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A. M. A.
Archives of Neurology and Psychiatry

VOLUME 77 MAY 1957 NUMBER 5

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Single copies of this and previous calendar year, $1.50.

Back issues older than two years are available through Walter J. Johnson, Inc., 111 Fifth Avenue, New York 3. Future reprints of back issues will be available through Johnson Reprint Corporation, 111 Fifth Avenue, New York 3.

Checks, money orders, and drafts should be made payable to the American Medical Association, 535 North Dearborn Street, Chicago 10.

AMERICAN MEDICAL ASSOCIATION Publication

Published monthly by the AMERICAN MEDICAL ASSOCIATION. Editorial and Circulation Offices: 535 North Dearborn Street, Chicago 10, Illinois. Publication Office: Thompson Lane, Box 539, Nashville 1, Tennessee. Change of Address: Notice to the circulation office should state whether or not change is permanent and should include the old address. Six weeks' notice is required to effect a change of address. Second-class mail privileges authorized at Nashville, Tenn., Aug. 6, 1956.

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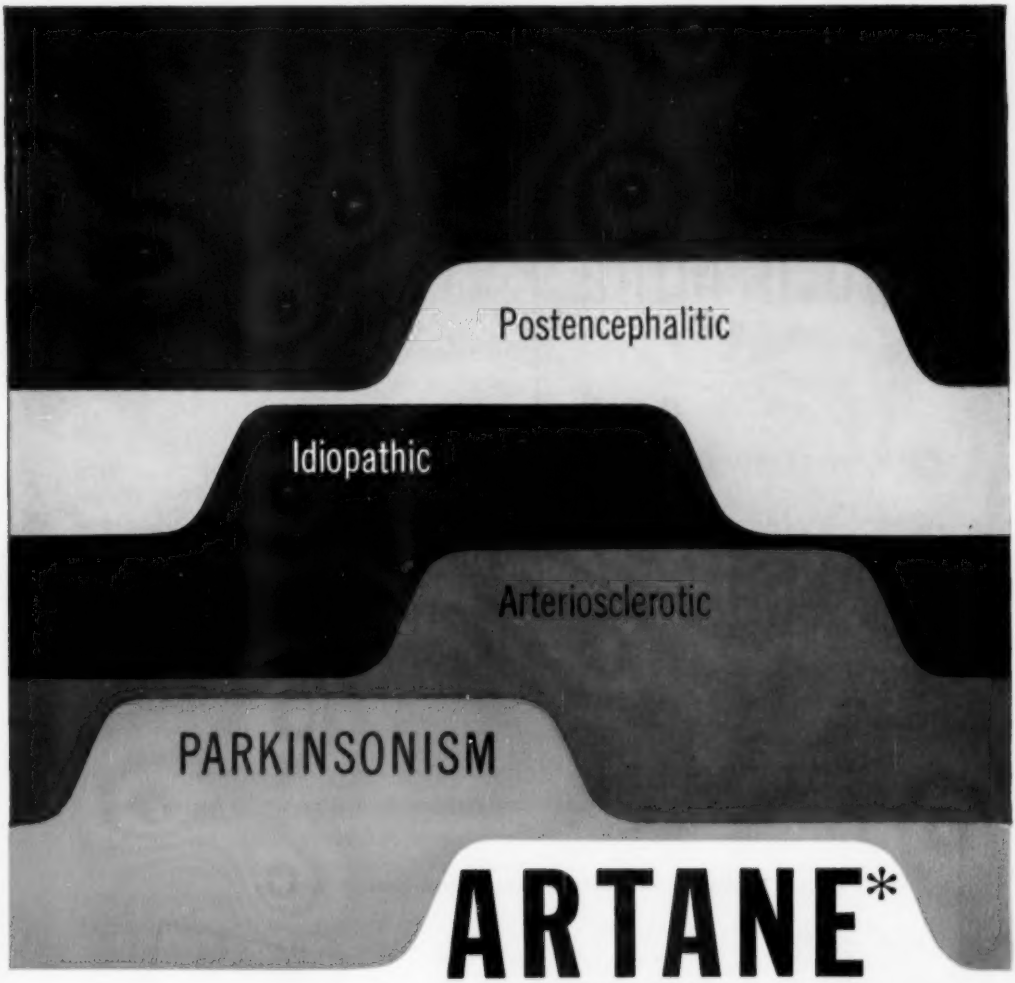

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SECTION ON
NEUROLOGY

Relationship Between Certain Forms of Psychomotor Epilepsy and "Schizophrenia"

I. Diagnostic Considerations

ERNST A. RODIN, M.D.; RUSSELL N. DeJONG, M.D.; RAYMOND W. WAGGONER, M.D., and BASU K. BAGCHI, Ph.D., Ann Arbor, Mich.

The description of "dreamy states" by Hughlings Jackson [1] in 1888 brought attention to the fact that a number of psychic symptoms could be experienced as a result of pathological events within relatively restricted areas of the brain. It could be clearly established in subsequent years that hallucinations, "bizarre" visceral sensations, feelings of depersonalization, sudden feelings of panic or impending catastrophe, distortions of bodily or spatial perceptions, loss of consciousness without convulsive movements, amnesic episodes, and automatic behavior can occur as a result of focal seizure discharges. Gibbs, Gibbs, and Lennox [2] described in 1937 a characteristic seizure pattern in the EEG which was frequently associated with the occurrence of these symptoms and suggested the adoption of the term psychomotor epilepsy. The studies of Jasper and Kershman,[3] Jasper and Penfield,[4] MacLean,[5] and Liberson [6] made it apparent that the focus of pathological activity is in these cases mainly in structures of the temporal lobe and its immediate anatomical connections, including the formations of the limbic system. For this reason the term "temporal lobe" seizures has come to be used more or less synonymously with "psychomotor."

Two factors soon emerged from the study of patients with this type of seizures. One was that these seizures represent the most frequent type of all convulsive disorders, and the other, that interictal psychiatric difficulties were by far more frequent in this group than in other epileptic patients. Gibbs [7] pointed out that these psychiatric disorders may be quite variable and the patients may appear paranoid, depressed, catatonic, or hysterical. Frantz [8] stated that symptoms referable to the sensorium are commonest: faulty perception, poor concentration, lack of cooperation, confusion, and somnolence, as well as changes in affect, intellect, and higher psychic functions. Magnus [9] emphasized that the patients who have these symptoms are, however, different from psychotic patients, since they usually realize that these feelings are abnormal and they do not identify themselves with them. Magnus therefore suggested that the hallucinations should be regarded as pseudohallucinations and the illusions as pseudoillusions. Mulder and Daly [10] suggested as differential diagnostic criteria the paroxysmal occurrence of these symptoms, their short duration, and their inappropriateness to the total situation.

Received for publication Aug. 2, 1956.

From the Neuropsychiatric Institute and Department of Neurology, University of Michigan.

Although these criteria are valid to a considerable extent, there exists a group of patients with which the clinician experiences marked difficulty—if all symptoms are taken into account—in deciding whether these are the expression of a psychotic, and especially a schizophrenic, process or the manifestations of a convulsive disorder. The symptoms and in most instances the personality background of these patients are usually such that a reasonable case could be built for either diagnosis. A recent report by Ervin and associates [11] also highlighted this situation. Of a group of 42 patients who had "temporal spikes" in the EEG, 34 (81%) received clinically the diagnosis of schizophrenia.

Since it is known that the diagnosis of schizophrenia rests at times to a considerable extent on a subjective impression of the examiner, and various examiners may apply different criteria, the above-quoted figure becomes, unfortunately, somewhat less meaningful.

For this reason six cases will be presented in some detail as to the symptoms and signs which these patients exhibited, and an attempt will be made to see whether or not the diagnosis of schizophrenia is applicable. It would seem reasonable to substitute in this discussion the term "schizophrenic reaction" as defined by "Diagnostic and Statistical Manual: Mental Disorders"[12] for that of schizophrenia. The "Manual" states that "this term is synonymous with the formerly used term dementia praecox. It represents a group of psychotic reactions characterized by fundamental disturbances in reality relationships and concept formations with affective, behavioral and intellectual disturbances in varying degrees and mixtures. The disorders are marked by a strong tendency to retreat from reality, by emotional dysharmony, unpredictable disturbances in stream of thought, regressive behavior, and in some by a tendency to 'deterioration'." If the patients fit these criteria, an attempt will be made to see whether Bleuler's fundamental and accessory symptoms of schizophrenia are discernible, and, thirdly, the cases may be checked against psychoanalytical concepts. If this should lead to the result that the symptom complex which these patients present could be called schizophrenic reaction, because all the mentioned criteria are fulfilled, one would then have to examine the question whether the association between temporal lobe epilepsy and schizophrenic reaction is one of chance occurrence, and the disorders are independent of each other, whether there exists a causal relationship in the sense that one is responsible to a major degree for the occurrence of the other, or whether they are both manifestations of the same underlying disease process.

Report of Cases

Case 1.—This 34-year-old woman came to the University Hospital in November, 1955, with the chief complaint of "epilepsy for the past 30 years." There is only a suggestive family history of a convulsive disorder, since some distant relative has had convulsions; however, the patient did not know any details. Nothing is known about the circumstances of birth and infancy. When the patient was 4 years old, her sister noted that she was thrashing about in bed at night, and the diagnosis of epilepsy was made at that time. She was put on anticonvulsant medication, with poor control of her attacks. The patient has subsequently had a variety of attacks, which are preceded by different sensations. During a light attack she may just "stare" for a period ranging from one-half to five minutes. In a severer attack she notices at first weakness involving the left leg and inability to talk; then she loses consciousness for a period of two to five minutes. During this time she does not fall but may just stand with flushed face, biting her cheek and occasionally losing control of her urinary bladder, or may shake all over or walk around aimlessly or run somewhere. After a severe attack she has difficulty in speaking for up to two hours. She states she can think straight but cannot get the proper words out; stammering or stuttering may continue even longer. Often she feels very tired after a seizure and may go to sleep for several hours. At times there is a different onset of the attack. She may suddenly experience severe crude fright or a sudden pain "like a sharp point going through the head." At other times she experiences a "buzzing sensation going through the left side of the body"; this may last an instant and be followed by loss

of consciousness or may last up to half an hour, during which time the patient also experiences difficulty in swallowing. At times there are auditory hallucinations present, which may be in form of a ringing, either like a churchbell or like a dinner bell which her mother used to ring. These hallucinations may come independently of the attacks. On one occasion, sometime after the death of her father, she had the hallucinatory experience of her mother's saying in a soft voice, "Daddy died," and recently she had heard the voice of her deceased father saying, "Daughter, you are next." This frightened the patient severely, since several members of the family had died during the past year. Visual hallucinations could not be elicited. The patient stated also that she has, in addition to the above-described attacks, episodes in which she suddenly comes to and does not know how she got where she is. Minor spells have been as frequent as one to six per day every day all of her life, as long as she can remember.

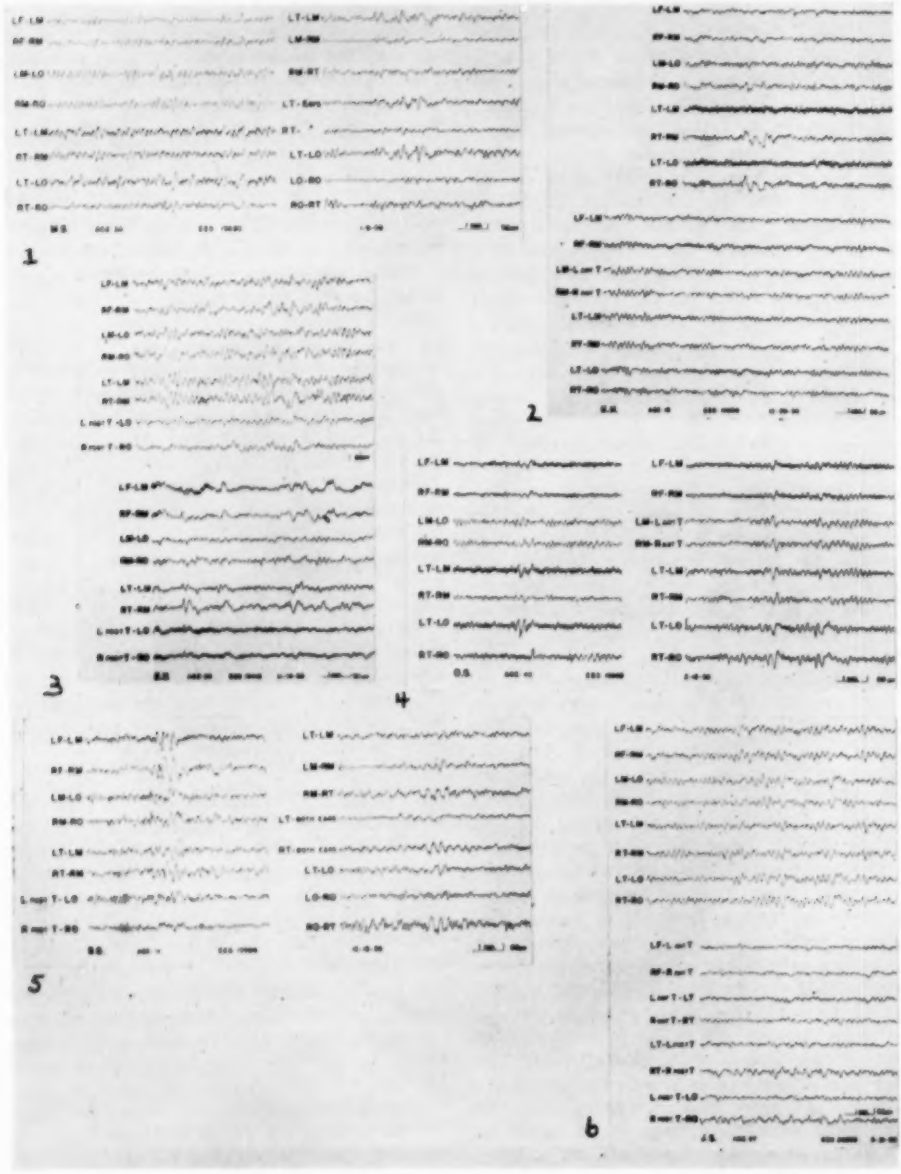
Since the patient was not seen in the department of psychiatry, the psychological test material will be presented in somewhat more detail. The patient earned a full-scale I. Q. of 104, with a verbal scale I. Q. of 104 and a performance scale I. Q. of 103. There was little scatter in the verbal area except for digit span, which was much lower than the other tests. It was thought that the difficulty here was apt to be due to anxiety interfering with attention. She did well in both comprehension and similarities. She failed only one arithmetic problem. In the performance area, picture completion and block design were high, while digit symbols and picture arrangements were low. The patient completed all block designs, working overtime on the last one. She was slow on digit symbols, which test involves the learning of new material. She did very poorly on picture arrangement and was inconsistent in that she arranged the easiest and most difficult series correctly. She had difficulty in grasping a total situation. The patient did well with the Bender Gestalt test. There were no distortions of designs. While there was a little carelessness, which could be regarded as due to organic brain damage, there was no marked evidence of organicity. During the Rorschach test the patient gave 82 responses, a number which was regarded as very high. She showed a great deal of fantasy living, and much of it was regarded as autistic. There were three alphabet concepts; a number of responses showed the presence of personal needs strong enough to distort perception and cause illogical thinking. She was noted to be emotionally immature in regard to her need to depend on other people and be loved by them, as well as in her expression of feelings, which was childish and impulsive. The findings were summed up by the psychologist in the following manner: The patient is a person of average intelligence. While the tests cannot rule out organic brain damage, there is no evidence that organicity is interfering with intellectual functioning. The Rorschach test shows a very immature personality pattern. The type of fantasy, the extent to which the patient indulges in fantasy living, and the amount of inaccurate perception point to schizophrenia. The seizures are not sufficient to account for the seriousness of the condition.

Academically the patient had done well. She had graduated from high school at age 19 and then taken one year of college. After that she quit school, owing to "lack of courses" which she desired. At present she lives at home with her mother, doing housework and apparently performing a competent job. She has never been married.

Clinical examination showed the patient's affect to be somewhat bland, but marked mood swings could be observed. Clinical neurological examination was essentially negative, with the exception of hyperactive deep tendon reflexes and a bilaterally positive Hoffman sign. Ophthalmologically, right convergent strabismus with amblyopia of the right eye was noted. The visual fields were normal. Routine laboratory studies were negative. The skull x-ray showed considerable thickening of the calvaria, which was thought to be within the realm of normal variations. An EEG showed high-voltage rhythmic 5 to 6 cps activity, mainly in the frontomotor and temporal areas, symmetrical on the two sides, and in addition in both temporal areas, but mainly on the left side, high-voltage sharp wave discharges (*Figure, 1*). At times they were seen independently on the right, but most of the time they were merely transmitted from the left temporal region. At times some 2 to 3 cps delta activity could also be observed in the temporal regions.

Case 2.—This 16-year-old girl was first seen at the University Hospital in December, 1955, because of "spells" since the age of 18 months. The family history revealed that the patient's mother is diabetic and nervous and faints frequently but has not had any convulsions. A paternal aunt has twin children, and one of these has convulsions. There are other members of the father's family who have had convulsions. The patient's birth was normal, but at the age of 18 months she fell down a basement stairs and hit her head on the concrete floor. No history relating to the seriousness of this head trauma or to a possible period of unconsciousness could be obtained. A short time following this accident the patient developed grand mal seizures. These were present for two years, then the patient was completely seizure-free for one or two years. Seizures recurred at the time that the

patient entered kindergarten and have persisted since. These seizures are of the typical grand mal variety, as well as minor ones. Grand mal seizures occur about once a month, occasionally two in one day; minor seizures occur every two or three weeks up to six a day. There are two main types of minor seizures—one during which she may black out momentarily, have a vacant facial expression, and drop things which she happens to hold in her hands. The second type may be regarded as the aura of the grand mal seizure since the patient does not know at the time of occurrence



1, Case 1; *2*, Case 2; *3*, Case 3; *4*, Case 4; *5*, Case 5; *6*, Case 6. Note the diffuse theta activity in all head areas and the focal disturbance in the temporal leads.

of the attack whether it will terminate spontaneously or go on to a full convulsive seizure. The aura may vary to a considerable extent. Most frequently the first symptom is flashes of lights, "like headlights of cars," coming toward her; the lights are in front of her, and not displaced to one side. At other times the aura may consist of "apparitions"; these are of a group of people or just one person; the faces then get all "distorted, ugly"; they come closer and closer; the patient by that time is very frightened and screams—the faces are also in the center, not off to one side—she then becomes blind and starts shaking, followed by jerking. At the time when jerking occurs consciousness is lost and she falls in a major seizure. The minor seizure ends with shaking. During the minor attack she can hear people talk but is unable to respond. There may also be auditory hallucinatory phenomena during the minor seizures, consisting of the voice of her mother yelling at her, and at other times a sympathetic voice, that of her aunt, who speaks in soothing tones. (In reality, both aunt and mother have witnessed numerous seizures, and this was their characteristic mode of reaction toward the patient at the time of an attack.) There may also be crude hallucinations of sound during the spell in the form of a "roaring, like sirens of an ambulance." This also gets louder and louder as the spell goes on, similar to the way in which the visions get larger.

After a grand mal seizure she is confused as to time and place for 5 to 10 minutes. She has headaches; when the confusion lifts, she is "real mean" to her mother, hates her intensely, and is bothered severely by whatever the mother may do. She is not aphasic but has some difficulty in speaking, mainly because of soreness of the tongue resulting from the seizure. There is at times some weakness of the right arm for several minutes. The patient usually lies down and sleeps then for several hours. After this there are no residuals, and she is her usual self.

In addition to the seizure history, a considerable interictal symptomatology is present; this the patient did not describe spontaneously, but it was readily ascertainable by appropriate questioning. Some of these symptoms are constant; others come and go; however, they are not in relation to the spells. A constant symptom is that she is "allergic to triangles"; after looking at one and then looking away from it, she can still see it plainly in front of her eyes for several seconds. This may also be true of pictures she has been looking at. If she has been looking at several triangles, they change shape and move around in a kaleidoscopic fashion. Other geometrical patterns, such as a cylinder, are not perceived as flat but are seen in three dimensions; "they stick out from the paper." At times she experiences momentary alterations of space perceptions; "angles look crooked"; micropsia may be present; "the telephone may look very small, but is normal to touch."

The patient then proceeded to relate several "visions"; these are not in the form of daydreams but have reality quality: "It's like a dream but yet more real than a dream." She sees herself frequently the way she looked as a baby; the baby looks at her in amazement, as if to say "My, have you grown!" There is nothing spoken during this scene. At other times she may see herself doing "a man's job," such as working in a heavy metal factory; she then wears boys' clothes. She is also believed to have prophetic qualities, since she has at times visions which allow her to predict future events.

Personalitywise, she stated that she "flies off the handle over little things." She gets along well in school, makes good grades, but was once referred to a child guidance center because she got angry with another pupil and chased this girl up and down steps, yelling that she would kill her if she would ever catch her. When asked about her relations to her parents, she stated, "I hate my mother; I don't know why, but I do. Mother is nervous and once tried to commit suicide by taking an overdose of sleeping pills." The patient is competent in the parents' home and does most of the work there. The father drinks alcohol excessively.

During the interview the patient gave a coherent story, and all the material described above is solely the patient's description. She was full of affect, and the mood swings were somewhat excessive; she cried easily and laughed easily; this was always appropriate to the situation. She always spoke fluently without blocking; only the stories about the "visions" were related very hesitatingly. Physically, she appeared plump and more mature than her chronological age. Clinical neurological examination was negative. Routine laboratory studies were normal. The skull x-ray revealed an asymmetric venous channel on the left side of the skull.

The EEG gave evidence of delta-theta abnormalities, and at times sharp waves, in the right temporal area, but also independent slow-wave activity in the left temporal region, as well as intermittently diffuse paroxysmal theta bursts (Figure *2*). During photic stimulation the patient became apprehensive and demanded that the light be shut off because it reproduced the sensation of "the car headlights getting bigger and bigger." There was, however, no objective change in the EEG, which could be regarded as a seizure pattern. Even after the photic stimulator was turned off, the patient

insisted for a period of 15 seconds that this was not the case, that she was still seeing the light flash. She never tolerated the light longer than a few seconds, then forcefully turned away or covered her eyes, thus not permitting a longer exposure, which might have resulted in electroencephalographic seizure patterns.

This patient was not seen by the psychiatry department.

Case 3.—A 23-year-old woman was first admitted to the University Hospital in June, 1955, because of generalized headaches and convulsions. The family history is negative for epilepsy or fainting spells. The father drank alcohol excessively and died of carcinoma of the throat when the patient was 12 years old. The patient's birth was supposedly uneventful. There was no history of severe trauma in infancy. However, during the first year of life, near the first birthday, she had four grand mal seizures in one day. There is nothing known about any concomitant illness. With the exception of frequent nightmares, which evoked in her the feeling of fear, "a feeling of helplessness and being overpowered," the patient had no seizures until the age of 17. At that time she started to date her present husband. He was sexually very aggressive and tried to have premarital intercourse. The patient consistently refused; however, "we became very intimate down there, but you know not to the point where a baby could have come." Her first seizure occurred in a study hall at school. The patient suddenly noticed that the teacher was sitting with crossed legs, and the thought went through the patient's mind, "Why does she sit in such an indecent fashion?" Then everything "became distant, far away, unreal"; her face got hot. This lasted only a few seconds, and there were no automatic movements. The following day the patient had a grand mal seizure. This started like the minor seizure but went on to a typical convulsion with loss of consciousness, tonic and clonic phases, and tongue biting. Grand mal attacks recurred from then on at infrequent intervals, usually not more than two a year. Minor seizures continued much more frequently, and there may be as many as two or three every day. They usually tend to come in groups; she notices some build-up of tension inside her until they occur. It takes the patient a full day to recover from the confusional after-effects. However, after a grand mal seizure her head "feels clearer" for a few days.

The minor seizures vary. At times she cries, "I feel funny." "God help me!" Sometimes she loses consciousness momentarily, at other times not. At times she has amnesic episodes, which may cover several hours of a day. During this period she performs work adequately but has no recollection of it. At other times she has spells which are described thus: "People become out of reach, unreal; they are far away, everything seems larger, very huge; you are too small, too weak; something was going to overtake you. Sometimes the bodies of people are distorted, like crippled, deformed like; the faces and heads are real huge; they stare at me, they have a sort of bewildered, frightened expression; the room where I am in sort of slants sideways, the left side is up, the right side is down; occasionally there is a bitter or salty taste present, no smell. I am afraid, complete fear all over, feel completely helpless, just as when, suddenly, someone very close to me has died."

The patient denied having auditory or visual hallucinations or changes in color perceptions.

While the grand mal seizures were well controlled by anticonvulsant therapy, the minor seizures were refractory to treatment. She also had, independent of the spells, prolonged déjà vu and *jamais vu* sensations, which might last for several hours.

During her hospitalization, a definite psychotic episode occurred two days after two consecutive grand mal convulsions. She became excited and confused, stood up in bed, cried, and tried to get out of the ward. Later, during the forenoon she calmed down somewhat, but during the afternoon there was definite evidence of hallucinations. She complained that she wished the voices would stop saying those things; they kept telling her that she was crazy; they were making fun of her; "The Lord told me I am cured." The following morning she was again rational and oriented.

Clinical neurological examination was negative; routine laboratory studies were also negative. There was no evidence of a field defect. The skull x-ray was normal, with the exception of some hyperostosis frontalis interna. The EEG revealed a focus of abnormal electrical activity, consisting of theta-delta discharges and at times sharp wave discharges in the right fronto-temporal area (Figure *3*). In addition, there was evidence of a more diffuse disturbance of cerebral function, since the background rhythm was slowed to 6 cps and was of high voltage.

The patient was seen in the department of psychiatry, and the following observations were made: "Affect shallow; many severe problems are described with an air of nonchalance. Complains of having been 'miserable' ever since her marriage. Husband is unfaithful, abusive, and dishonest. Demands unusual sexual practices and when refused overpowers her forcefully. Patient's father drank heavily and was brutal to wife and children; she feared him until his death. Patient's sister had a psychotic episode at age 15. The patient was always unhappy as a child because of extreme

self-consciousness, felt that others looked down on her, and thought that when she could see people talking but couldn't hear them that they were talking about her. The patient has attempted suicide on several occasions. She notices a clicking in her spine and has headaches which feel like "electricity." She is concerned about her children, especially that the oldest will strangle the youngest. The oldest child has temper tantrums, holds his breath until he gets blue when angered, and sometimes loses control of his bladder doing it. It was the psychiatrist's impression that the patient functions on a low level, a finding which could not be explained by organic impairment of her intellectual functions, since this seemed minimal. She was regarded as an infantile masochistic person presenting many hysterical features, and it was added that beneath the hysteria probably lies schizophrenia.

Psychological testing showed some signs of organicity on the Bender test. While the Rorschach test gave no evidence of brain damage, the personality pattern was found to be immature for an adult and more the type expected from an adolescent. Both schizoid and depressive features were present in the record; some illogical thinking and morbid thought content were noted, as well as a tendency to form an autistic and unrealistic relationship toward the world.

Since the minor seizures were uncontrollable by anticonvulsant medication and the patient was totally incapacitated by them, a right temporal lobectomy was carried out in November, 1955. Electrocorticography and depth electrography during the operative procedure revealed that the focus of abnormal electrical activity extended far into the posterior temporal region and could thus not be excised *in toto*. The anterior portion of the temporal lobe was removed up to the vein of Labbé (about 6 cm. from the tip of the temporal lobe). The excised tissue revealed microscopically loss of ganglion cells and increase of glial elements (astroglia). Silver preparations showed diffuse gliosis throughout.

The patient withstood the operative procedure well. There was initially some decrease in the frequency of minor seizures; however, at a recent examination it was apparent that there had been no remarkable benefit from the surgical procedure. There was no change in her psychiatric symptomatology.

Case 4.—This 42-year-old woman was seen for the first time at the University Hospital in May, 1949, with the chief complaint of headache. Investigation at that time revealed that the patient has had "fainting spells" since infancy. The patient is unconscious during the spell; she has no warning but falls to the ground and has repeatedly hurt herself while doing so; there is no typical tonic or clonic phase. The spells may occur at any time during the day or night. The patient was told by her husband that when they are nocturnal she moans, then "struggles" for about a minute, and following this is limp.

The family history is negative for seizures, and birth and early childhood were supposedly uneventful. At the age of 21, while attempting to roller skate, she fell and struck the back of her head on the concrete sidewalk. She was unconscious for two hours. X-rays were not obtained. Her headaches dated back to this accident. The black-out spells increased in frequency up to two or three a day around 1943; at times she did have a warning in the form of a hot flash. In addition to these, she has spells during which she wanders around in an automatic fashion, with no recollection afterwards. Once she drove about 14 miles in her car during a trip, with amnesia for this period. She had handled the automobile apparently correctly and had been driving through the state capitol during the period of amnesia. There was only one grand mal convulsion, and this occurred when the patient's first child was born.

In addition to the above-described seizures, considerable other episodic symptomatology is present. There is occasional twitching of various muscle groups of the arms and legs and dizzy spells, during which she feels shaky; she sees "stars before her eyes," and things seem to float in the air before her; she experiences continuous nervousness and episodic crying, for no good reason. At times there are visual hallucinations, which allow her to predict future events. She had attempted to commit suicide on two occasions, once by swallowing a saponated cresol solution (Lysol) on another by taking an overdose of barbiturates.

Clinically the patient was found to be obese. There were no abnormalities on the neurological examination. Routine laboratory studies were within normal limits. Ophthalmological examination gave no evidence of a field defect. The electroencephalogram showed medium- to high-voltage rhythmic 6 cps activity, which occurred in generalized bursts, lasting one-half to one second. There was, however, no definite focus of abnormal activity. A skull x-ray was negative, and a pneumoencephalogram suggested minimal left-sided cerebral atrophy. The patient was then placed on diphenylhydantoin (Dilantin) and phenobarbital medication and dismissed from the hospital.

She returned in March, 1956, because of increase in nervousness, increase in spells, and more frequent headaches. She attributed these to the husband's demand for unusual sexual practices. The seizures had been under fair control with the anticonvulsants mentioned, and she had noted that

she usually developed a "funny feeling," a "full feeling" in the head, about one or two days prior to a seizure. At times she was able to avoid an attack by increasing her diphenylhydantoin dose at that time. Lately the attacks have changed somewhat, inasmuch as she does not black out completely during the seizure but has some awareness of what is going on. During the seizure she is limp and unable to move or talk; it lasts usually about two minutes.

The other symptoms which have been described above were not influenced by the anticonvulsants. The patient then related additional episodic disturbances. She experienced a ringing in the right ear, like a telephone ring, and she has given up answering the telephone lately unless there is someone else in the room who requests her to do so, because, as she said, "I've been fooled too often; I go there, pick it up, and there's nobody on the line." At other times, when driving in a car, she hears occasionally the sound of a horn, as if another car wanted to pass. In addition to these crude auditory hallucinations, there occurs at times a more elaborate one. This is usually after a spell, and she hears someone's voice—she believes this to be her guardian angel's—saying, "Don't worry; you're gonna be all right." This voice comes always from the right side and has never said anything else but this particular phrase. The experience is, however, very vivid, and she has frequently become annoyed about it, "because I don't need anybody to tell me that I'm gonna be all right, I'm all right by that time anyway"; and she has at times attempted to "brush this little fella off" from the shoulder with her left hand. This had no influence on the hallucination, however, and it usually disappears spontaneously when she goes to sleep. There have also been intermittent visual hallucinations consisting of seeing a bug crawling on the window or little purple spots moving in the right field of vision.

Psychiatric examination showed that the patient's speech was fluent, relevant, and coherent. There were marked swings in affect; she was continually extremely preoccupied with sexual matters, much of which was regarded to be delusional. She was oriented and her memory appeared intact; however, abstract reasoning and thinking appeared impaired. During psychological testing the patient was more eager to talk of her clairvoyance than of her symptoms; she was suspicious and hostile all through the test. Her full-scale I. Q. was found to be 118, verbal I. Q. 106, and performance I. Q. 128. She showed a fairly stable superior performance, but on the verbal scale the patient presented considerable variability with occasional lapses of judgment. The Bender performance was poor and characterized by lack of planning and half-hearted execution. The Rorschach was filled with sexual material which was thought to be representative not of responses given usually by people with sexual preoccupations but of more perverse oral sadistic concepts. Structurally the record was regarded as very poor with markedly defective form quality. The sentence completion test showed markedly exaggerated narcissism. It was the impression of the psychologist that the patient was a profoundly regressed person and that all categories applied to her: pseudomasochistic; narcissistic; hysterical; polymorphous perverse. She also seemed subtly delusional and decompensated to the point where a paranoid schizophrenia appeared likely.

Clinical neurological examination and routine laboratory studies were still negative, and the EEG showed still marked paroxysms of medium to high voltage, which were maximal in the temporal areas, as well as high-voltage, sharp discharges occurring independently in the temporal regions (Figure, *4*).

Case 5.—This 11-year-old girl was admitted to the children's service of the Neuropsychiatric Institute in May, 1955, because of psychotic behavior. The parents noted some evidence of difficulties around Christmas, 1954. The patient then complained intermittently of dizzy spells and headaches. Seven weeks prior to admission she developed peculiar motions, which led the home doctor to suspect the presence of chorea. In addition, she began to giggle in a silly manner, was concerned that boys were watching her in the bathtub, and reported seeing animals with big ears, some vague shapes on the walls, and hearing voices. These voices accused her of misbehaving with boys. She exhibited also much concern about her clothing and felt that people were accusing her of having stolen it. On admission she was clearly out of contact and appeared to be hallucinating continuously. The hallucinations were not stereotyped; they bothered her most when she was not occupied. When her interest could be aroused, they disappeared. At times she could be stopped from talking back to the voices by firm commands. Her behavior was aggressive at times, and she masturbated freely. She was also seductive to the male staff. On the ward the patient complained frequently of "dizzy spells." These were described by her thus: "Well, I would just get dizzy, like I just ran around in circles, I would get dizzy." At times she vomited during these spells, which lasted several minutes. She also complained at times of "dirty pains in the stomach," "dirty pains in my head," "dirty pain in my bust." At times she was observed awakening at night out of sound sleep with the complaints, "Oh, my stomach pains," pointing to the epigastric region

and left chest, and "I feel so sick, I have a dirty pain in my head." She appeared confused during that time, coughed, and giggled, and the face appeared flushed. These episodes lasted several minutes. Similar spells also occurred during the daytime. The patient had both visual and auditory hallucinations. The visual hallucinations were either crude, consisting of dots and lines, or formed animals in various shapes. They were most pronounced during the evening when the room lights were turned off, and the patient insisted always that a light should remain on in the hall. Samples of her auditory hallucinations follow. The patient would go to a nurse and say, with a troubled expression on her face: "I hear these voices that tell me that I shouldn't be crying; they say something must be wrong with me. Could there be people in other rooms I could hear talking"? At times she heard a boy's voice saying "bong" over and over again. At times she asked: "Can people hear what other people think? I keep seeing kids from home in cars, and they talk about things I'm thinking and I can hear their accents; and home is 450 miles from here; so how can I hear their accents?" Once when asked to describe her voices, she stated: "They talk soft—it seems like I can hear somebody say 'Does your sister have a guilty conscience; does she have a guilty conscience?' They are not asking; they are saying. They seem they're not real—they seem artificial . . . . If someone tells you they are your imagination, it seems they ought to stop." "The night before last, in the motel, they said, "Don't turn around or you will see something. I'm going to come in bed and stab you. I am going to stab you." "I don't know; I think it's my imagination, but it seems sort of queer. Today they seem lighter; they used to talk real loud—now they talk lighter—lower, I mean." She slept very poorly most of the time and complained that the voices kept telling her to get up. The patient had a monotonous, somewhat whiny voice. Her affect fluctuated between anxiety, depression, and giggling.

The past history was essentially noncontributory. There was no family history of convulsive disorders. The maternal grandfather died at a state hospital, to which he had been committed at 60 years of age. There were no difficulties at birth, no history of significant head injury, and no serious illnesses during childhood.

Her physical examination was normal with the exception of some obesity. The routine laboratory studies were within normal limits. A skull x-ray was regarded as negative and a pneumoencephalogram as within the limits of normal. The over-all size of the lateral ventricles was thought to be at the upper limits of normal. The EEG showed a mixture of delta and theta activity, mainly in the temporo-occipital regions, more pronounced on the right than on the left, and during drowsiness paroxysms of high-voltage diffuse atypical spike-wave discharges, lasting about one second. Hyperventilation effort was poor, and no spell was induced (Figure, *5*).

Psychological testing was carried out on several occasions. The patient achieved a verbal I. Q. of 96, a performance I. Q. of 90, and a full-scale I. Q. of 93. These scores were taken to indicate average function. Regardless of the overt disorientation and confusion, the Bender Gestalt test was intact. On the Rorschach examination some sporadic breaks in reality testing were found but—the psychologist added—not the pervasive disorganization that one would expect. There was no evidence that ego boundaries were confused. Anxiety was intense and uncontrolled. Outstanding in the record of a child of her age was the evidence of sexual preoccupation. Attitudes of evasion and guardedness, as well as stubbornness and negativism were also noted. In conclusion it was thought that the record was not typical for an 11-year-old child, but that it more clearly resembled the hysterical patterns as produced by an adult. Another Rorschach examination after three months of psychotherapy and the intermittent use of chlorpromazine (Thorazine), amphetamine (Benzedrine), and α-4-piperidyl diphenyl carbinol hydrochloride (Frenquel), revealed a "gradual disintegration of her defenses. Intellectually she had lost her capacity for adaptive thinking. Her thinking was dissociative. Affectively she was much more volatile, and her capacity for mature object relationships was lessening. Her negativism was increasing. She remained sexually preoccupied. Ego boundaries were decreasing." The results were regarded as prognostically unfavorable. It was added that "the breakdown of adaptive thinking, the elated mood, suggest that this youngster is not responding to specific therapeutic techniques and will undoubtedly have to be committed to a state institution for long-time care."

Case 6.—This 26-year-old man was first seen in the neurology department of the University Hospital at the age of 14 because of "convulsions." At the age of 6 years he fell from his tricycle and struck the left side of his head. He suffered a severe contusion and was taken by ambulance to the hospital. On the way to the hospital it was noted that he "trembled all over" for a few minutes. He was unconscious from the time of the accident, at 5 p. m., until the next morning at 9 a. m. Skull x-rays were negative at that time. He remained in bed for six weeks after the accident because of an elevated temperature. One year later he began to develop spells which were

preceded by epigastric discomfort; then tonic and clonic movements of the right arm could be observed, and at times hyperextension of the right leg. The head and eyes turned to the right. Consciousness was narrowed and at times absent. In severe spells loss of bladder control occurred. These attacks lasted usually 5 to 10 minutes and were followed by listlessness, headaches, and at times numbness and weakness of the right arm. Occasionally the patient had mild attacks during which he was listless and some smacking movements of the lips could be observed. These lasted usually two to three minutes. At times he had "quick spells" during which he felt "funny," would get up, leave the room, and go to the bathroom, not remembering anything when he came back. These "slight black-outs" he had sometimes daily, and occasionally several in one day. At times the spells were so minor that onlookers might not have recognized that he had one. On occasions simple faints without convulsive movements occurred. There was also evidence of automatic behavior. For instance, he would get on a bus and get off again, after three blocks, then regaining consciousness. Once, during a history examination, he stood up, walked to the door, came back, and finished the test, with amnesia for the event. He received a "B" in the course.

General physical examination was negative. Clinical neurological examination revealed hypotonia and slight weakness of the right arm, a positive sign of Babinski on the right, and a questionable Babinski sign on the left. There was also an abortive ankle clonus noted on the right. A skull x-ray was negative. Lumbar puncture gave normal results, and a pneumoencephalogram showed relatively large ventricles but was otherwise normal. In subsequent years the patient was tried on a variety of anticonvulsive medications with reasonable control of his seizures. He was supposedly completely controlled for the past 15 months prior to the present admission on a combination of diphenylhydantoin (Dilantin), phenobarbital, phenacemide (Phenurone), and primidone (Mysoline). Phenacemide had been started in 1949, and the patient had never had any side-reactions despite continuous treatment. Primidone was added in January, 1955.

Fourteen days prior to the second admission the patient started to complain that people were talking about him, that at work everybody was egging him on and "torturing" him. He was suspicious that there were microphones planted around the house. He felt that the two telephones in the house were there in order to get messages on him. He also believed that his father—who is a police officer—was using Secret Service measures to investigate him. The patient gave up eating and, when asked why, stated that he had heard that in Spring and in fall people get ulcers and "you won't get ulcers if you don't eat," and therefore he was not eating. He came spontaneously to the hospital in order to have his routine medication check-up. It was immediately apparent that he was confused, could not give a coherent story, grinned inappropriately, and stared into space intermittently as if hallucinating. Examples of the patient's thought processes follow. When asked whether he had any difficulty in sleeping, he answered that he slept well, then added: "It's a lighter sleep than I usually have; it's just that it's easier to wake up in the morning; is that what you mean? I'm not tired to begin with, so I don't sleep any length of time; then I wake up." When asked about daydreaming, he remarked: "One type is a fantasy, I just don't know what you mean; there is a kind of daydreaming that is fantasy; I don't know, I don't know exactly what they mean when you get to the definite term." When asked if he experienced any difficulty in thinking, the answer was: "Difficulty thinking? What do you mean by that? No (giggled), no; I don't have any trouble thinking. No (giggled); that's it for that type of question; no."

Clinical neurological examination was normal. The patient was seen in the department of psychiatry, and it was noted that he was anxious in the interview, grossly inappropriate, guarded, hostile, delusional, circumstantial, and irrevelant and seemed confused. He was, however, oriented as to time, place, and person. He lacked insight completely. During psychological testing the same behavior was noted. Only the Wechsler Bellevue and the Bender Gestalt test were administered. His affect was regarded as shallow. Although it was thought that the patient was of superior intelligence, he was able to score only 119 on the verbal scale and 106 on the performance scale. The full-scale I. Q. was 115. There was thought to be little or no evidence to suggest the presence of an organic brain syndrome, although the patient experienced some mild difficulty with the block designs. He was regarded by the psychologist as clearly schizophrenic.

Routine laboratory studies were within normal limits, with the exception of a positive Ehrlich urobilinogen reaction of a urine sample and a thymol turbidity of 3.2 units. Cephalin flocculation test was negative.

The EEG showed diffuse theta activity in frequencies between 5 and 6 cps, which had entirely replaced the alpha rhythm. In addition, there were in both temporal areas, independently, but more pronounced on the right, sharp wave and delta discharges to be seen (Figure, 6).

Comment

In reviewing these cases, one gains the impression that a schizophrenia-like symptomatology can be discerned to a varying degree in all of them. This may be so outspoken as to make the diagnosis virtually certain on clinical grounds alone (Cases 5 and 6), or it may be somewhat more subtle, and discernible mainly on psychological tests (Case 1). Cases 2 to 4 could be regarded as showing moderately severe disturbances. The diagnosis of schizophrenia would in these latter cases probably depend on the orientation of the examiner. The question remains, however, whether there is evidence to the effect that the term schizophrenic reaction could be applied to all cases. This question can be answered affirmatively if the patient's minor "spells" and immediate after-effects were regarded of psychogenic origin. These could then be interpreted as "regressive behavior," "unpredictable disturbances in the stream of thought," or "fundamental disturbances in reality relationships," as outlined in the "Diagnostic Manual." Bleuler's fundamental symptoms of schizophrenia were outstanding mainly in Case 6 (especially disturbances in association and loss of affectivity), while the accessory symptoms (hallucinations, delusions, fragmentation of the personality, and somatic symptoms) were outstanding in the other five cases.

Fenichel [13] formulated the main concepts of the psychoanalytical point of view as follows:

> The psychotic escapes a conflict with reality through breaking with reality. He represses not the instinctual impulse which leads to conflict but the perception which stands in the way of his wishes. This break with reality follows a regressive path, the patient sinks back into that state in which he lived before acquiring the functions of reality testing.

He points out also that "the psychological process that leads to the development of a schizophrenic psychosis begins with narcissistic regression and the psychosis consists partly in the manifestations of this regression and partly in expressions of the remaining, objectively oriented part of the personality to counteract the process of regression." It is apparent that the application of these concepts could legitimately lead in our cases to the diagnosis of schizophrenia, since there is ample evidence of "narcissism," "regression," and "breaking with reality."

From a neuropsychiatric point of view these cases offer a fascinating problem. Psychotic and convulsive phenomena are in these instances so interlaced that it is in part very difficult to say on clinical grounds alone which symptoms are due to seizure discharges and which are "psychotic." The electroencephalogram assumes, then, a large role in confirming the convulsive nature of a sequence of symptoms, "bizarre" as they may sound when the patient tries to put his experiences into words. It is, however, valid only in a positive sense, and absence of visible alteration of the surface EEG while the patient experiences a symptom does not preclude the presence of seizure discharges in deep structures which do not reach the surface of the cortex. In this connection Bleuler's [14] clinical findings are also of interest. He stated that "epileptiform attacks may appear [in schizophrenia] at any stage of the illness. These may remain isolated phenomena or may repeat themselves over a period of years." He also added that "some abortive attacks can not be differentiated from petit mal attacks." The examples which are then listed make it apparent that we would regard these seizures today not as petit mal but, rather, as belonging to the psychomotor variety. The advent of electroencephalography confirmed these clinical impressions, and Hill [15] brought evidence that a definite affinity exists between epilepsy and catatonic schizophrenia. Karagulla and Robertson [16] came to the conclusion that there may be a neurophysiologic basis for schizophrenia, since epileptic discharges and cortical stimulation can evoke gradations in the intensity of hallucinatory experiences similar to those in schizophrenia.

At this point it appears legitimate to ask whether the clinical finding of prevalence of psychotic symptoms in patients with temporal lobe epilepsy is a chance occurrence of whether this could be expected from known neurophysiologic data. Papez [17] suggested in 1937 that the anatomical structures of the rhinencephalon may be important relay centers for emotional behavior. Subsequent animal experimentation by MacLean,[18,19] Kaada,[20] Liberson,[21] and others proved this concept to be valid. Experiments involving electrical stimulation of these structures in the conscious human by Penfield,[4] Liberson,[6] Delgado,[22] and others also produced marked changes in visceroautonomic as well as psychic functions.

The dramatic change in behavior of monkeys after bilateral temporal lobectomies, as demonstrated first by Klüver and Bucy,[23] was likewise a milestone in neurophysiologic research. The syndrome which was produced consisted essentially of psychic blindness (the animals could see but did not recognize objects); strong oral tendencies, to the extent that all objects, even noxious ones, were approached with the mouth; an excessive tendency to attend to every stimulus; a remarkable decrease in aggressive behavior and loss of fear reactions; increased sexual activity, and voracious appetite (which included the ingestion of inedible material and meat). Evidence has been presented recently that the same syndrome, with the exception of oral tendencies, can be observed in man if both temporal lobes are removed. It should be remembered, however, that it occurs either in animal or in man only if bilateral ablations are performed. Unilateral ablations are ineffective. Terzian and dalle Ore [24] stated that the most striking changes in his 19-year-old patient consisted postoperatively of a complete loss of recognition of people, even close relatives; an increase in sexual activity in form of masturbation several times a day and homosexual tendencies; a voracious appetite, and serious deficiencies of memory. It should be pointed out that the negative findings are also of importance. The patient was not aphasic and had no gross motor or sensory defect and no disturbances in coordination.

On the basis of these studies it would be reasonable to assume that the integrity of the temporal lobe structures and their subcortical connections is vital for an adequate functioning of the personality. If the functions of both temporal lobes and their associated areas in the frontal lobes, as well as their subcortical relay stations, are severely interfered with, as demonstrated by electroencephalography, one might be able to predict, from the appearance of the EEG, that this patient is likely to have severe "emotional" difficulties.

In our Case 3 the excised tissue was examined microscopically and it revealed gliosis and loss of ganglion cells. This is in keeping with findings obtained by Penfield's group of workers. The patient's symptoms could thus be regarded as the expression of loss of function of certain areas plus the result of constant irritation of the remaining healthy cells due to gliosis. This irritation could give rise to the vague visceral sensations which may appear either as protracted or in sudden spells (depending, in part at least, on the degree of the intensity of the stimuli). The hallucinatory symptoms may likewise be viewed as symptoms of irritation. Whether the experience is regarded by the patient as "reality," or "like a dream" or "like a thought," or as a clearly pathological occurrence from which he can dissociate himself may, again, depend on the intensity of the stimulus, and probably also on the adequate function of the other temporal lobe. Furthermore, the premorbid personality structure would probably also be of considerable influence. While we could thus understand the occurrence of "a hallucination," the content of the hallucination is different for each patient and becomes understandable on the basis of his life experience and psychodynamics. It could be pointed out in connection with a previous

publication by one of us (E. A. R.)[25] that the content of the hallucinatory material and occasionally of automatic behavior produced by seizure discharges may be just as meaningful for the patient as if this were the result of a psychogenic conversion phenomenon. It is worth emphasizing in this connection the point which was raised by Whitehorn,[26] that "meaning" and "cause" should not be confused with each other.

There is thus some evidence to suggest that certain patients with schizophrenic reactions may actually suffer from an organic process involving the temporal and related structures. It could be hypothesized that initially the irritative-convulsive manifestations may be prominent. This could also give rise to the intense anxiety which these patients experience. Later in the course the destructive element and loss of functions may be more apparent. The affect becomes flat, and the patient may then present in a mitigated form a picture somewhat reminiscent of the Klüver-Bucy syndrome.

As it is apparent that some cases of temporal lobe disease are very difficult to differentiate clinically from the process of schizophrenia, it would seem worth while to start at this juncture of our knowledge to follow a suggestion by Hoch [27] and separate these cases from other groups of schizophrenic cases in which no evidence of gross "temporal lobe" disorder can be found. It may be suggested that the term schizophrenia be abandoned for the present and be replaced by the term schizophrenic reaction, to which is then added "associated with 'temporolimbic system' dysfunction." This term would imply that the structures of the limbic system * and of the temporal lobe, including the island of Reil, are mainly involved in an active disease process. This group of symptomatic schizophrenic reactions could then be contrasted with a group of schizophrenic patients in whom, with present-day methodology, no evidence of significant aberration from normal physiology can be found. This second group might then be classified as "idiopathic schizophrenic reactions" until further knowledge develops. It appears likely that, in addition to the symptomatic group which is described above, other symptomatic groups exist which may be detectable if the diagnosis of schizophrenia is no longer regarded as an end-point which eliminates further diagnostic studies. This classification would have the advantage that one group of patients could be studied separately, and thus more accurately. The diagnosis, although still descriptive, would nevertheless be somewhat more concise than at present. It would also allow one to take cognizance of the observations in depth electrography which revealed "spike" activity in some "nonepileptic" schizophrenic patients.[28,29] A careful and detailed history on these patients might well show the episodic seizure symptomatology, which might be unnoticed otherwise or be regarded as psychogenic.

The concept of separating the "idiopathic" from the "symptomatic" group of schizophrenic reactions not only could prove fruitful in our search for more specific causative agents but could also at present influence our therapeutic techniques. These therapeutic considerations will be presented in a subsequent publication.

* The limbic system, as suggested by MacLean,[18] consists of the cortex adjacent to the olfactory striae; the pyriform area; the hippocampal gyrus and hippocampus; the parasplenial, cingulate, and subcallosal gyri, and the subcortical cell stations, which include the amygdala, septal nuclei, hypothalamus, epithalamus, anterior thalamic nuclei, and parts of the basal ganglia.

Summary

It is again emphasized that patients with a "psychomotor" type of convulsive disorder may present additional symptoms which are frequently regarded as psychotic, and especially schizophrenic.

Six cases are presented in some detail to illustrate this point. Various degrees of "schizophrenic" symptomatology can be discerned.

All cases had EEG evidence of disturbance of function in the temporal lobes and deeper structures.

If typical grand mal seizures are not pronounced, it is possible to regard the minor seizures of these patients as psychogenic in origin and arrive at the diagnostic conclusion of schizophrenia.

It is suggested that for the term schizophrenia should be substituted that of schizophrenic reaction. These schizophrenic reactions could be divided into a "symptomatic" and an "idiopathic" group.

The above-described patients could be regarded as part of the symptomatic group and the condition classified as schizophrenic reaction associated with "temporolimbic system" dysfunction.

This classification would enable one to understand better the occurrence of epileptic-like EEG patterns which can be obtained by surface recording, depth recording, or activation studies in some patients with "schizophrenia." It could also lead to a somewhat different therapeutic approach.

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Intracerebral Hematoma

Its Pathology and Pathogenesis

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Hemorrhage into the substance of the brain is one of the commonest lesions of the human body, being eclipsed, insofar as the central nervous system is concerned, only by occlusion of a major arterial channel. In the great majority of cases such hemorrhages are the result of rupture of an arteriosclerotic vessel, being precipitated by an elevated blood pressure. Other essential causes of intracerebral arterial rupture, such as trauma, embolism, ruptured aneurysm or vascular anomaly, blood dyscrasias, and syphilis, are relatively rare.[1] Occasionally one encounters a case in which no cause for the hemorrhage can be found. In general, cerebral effusions may be subdivided into traumatic and "spontaneous" groups.

The onset of cerebral symptoms following hemorrhage is usually acute and immediately consequent to rupture of the diseased or injured artery. However, in many instances, particularly those consequent to trauma, evidence of hemorrhage may be delayed for hours or even days. The term "delayed traumatic apoplexy," in the sense of Böllinger,[2] is then often applied to describe the situation. In this group of cases the hemorrhagic effusion is much more likely to be found in the frontal lobe or in the temporo-occipital region.[3]

Received for publication June 25, 1956.

Read before the Section of Nervous and Mental Diseases at the 105th Annual Meeting of the American Medical Association, Chicago, June 13, 1956.

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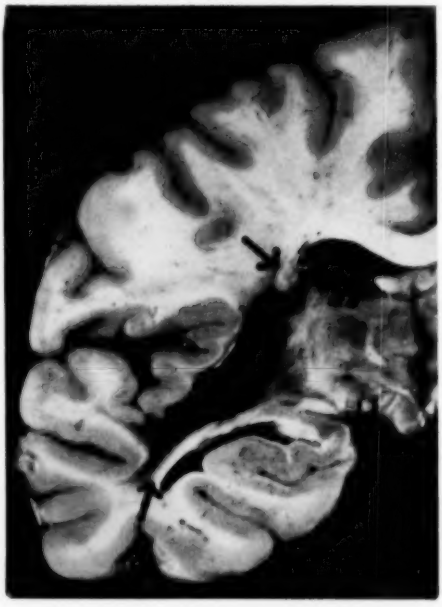
In any case, the outcome of the hemorrhage is dependent largely upon its size and location. Death usually follows shortly after gross effusions, particularly when there occurs a rupture into the ventricles or, less often, to the exterior. Smaller extravasations, especially those into the lateral ganglionic region,[4] are more apt to be survived, with the characteristic spastic hemiplegic syndrome. In such instances there follows a progressive breaking down of the clot, with a characteristic sequence of color change and absorption of the products of degeneration, with coincident shrinkage of

Fig. 1.—Residual cyst of ordinary spontaneous hemorrhage into external capsule exemplary of usual late result of such effusions. Note that cavity is somewhat removed from body and inferior horn of corresponding lateral ventricle (arrows).



the hemorrhagic cavity. Ultimately, there remains a narrow, contracted, slit-like defect with an irregular pigmented lining (Fig. 1).

"Interval Syndrome" with Intracerebral Hemorrhage

On the other hand, after an appreciable interval following a "stroke," there occasionally develops a syndrome of increased intracranial pressure. The patient appears to recover to some extent from the original insult, insofar as his lucidity is concerned, and perhaps also to a degree from the attendant hemiplegia. But with the passage of time he begins to complain of headaches of increasing severity and of blurred vision, then becomes lethargic, and ultimately lapses into a state of stupor. Examination discloses swelling of the optic discs and, if a lumbar puncture is done, an elevation of cerebrospinal fluid pressure. This state may also appear after a craniocerebral injury (particularly those incident to traffic accidents and falls). Under these circumstances, an "interval" dural hemorrhage is suspected. In either case, an exploratory cerebral puncture, properly directed, will result in the evacuation of bloody fluid mingled with clots, usually with relief of symptoms.

This clinical state is now generally recognized to be the result of an "encapsulated" collection of blood within the cerebral centrum, or ganglionic region, on which basis the term of intracerebral "hematoma" has been proposed. The lesion has been compared to a subdural hematoma, not only because of the resultant "interval syndrome" produced by it, but also because it is presumed that the original collection of blood has become "encapsulated."[5]

Intracerebral Hemorrhage vs. *"Hematoma."*—A survey of the literature makes it obvious that the issue as to the possible residuals of intracerebral hemorrhage is confused by a failure to distinguish between a more or less relatively "dry" blood clot, on the one hand, and the progressively enlarging, fluid-filled blood cyst, on the other. There is no reason for considering the first lesion, a slowly shrinking blood clot, as an indication for surgical intervention. Removal of the deteriorating clot does nothing to improve the patient's condition. An entirely different situation exists in case of a progressively enlarging hemorrhagic cyst. Evacuation of the fluid, particularly of the original clot, is important in terminating the syndrome of increasing intracranial pressure. This lesion alone is entitled to the designation of an intracerebral "hematoma."

It is the purpose of this study to make absolutely clear this distinction between the residual, progressively shrinking blood clot following the majority of cerebral hemorrhages and the so-called intracerebral "hematoma." The essential differences in the evolution and structural changes in the two lesions will be pointed out, and a theory as to the pathogenesis of the "hematoma" will be introduced. The problem will first be considered in the light of the recent literature on this subject.

Intracerebral Hematoma in the Recent Literature

Judging from the discussion provoked when the subject of intracerebral hematoma is presented, it must be presumed that many neurosurgeons with any extended experience have encountered, perhaps inadvertently, the residuals of ordinary intracerebral hemorrhage. As has already been pointed out, such effusions sometimes follow rupture of diseased or abnormal blood vessels. In other instances, however, the intracranial space has been explored after the development of a typical "interval syndrome" following cranial injury on the presumption of the presence of a subdural hemorrhage.[6]

In many cases the interval between the development of signs of increased intracranial pressure and the original vascular effusion has been so prolonged as to raise serious doubts of any possible connection

with it. The patients so affected are therefore often treated as "intracranial tumor suspects," and the nature of the lesion is recognized only when the hemorrhagic cyst is exposed by puncture or incision through a flattened convolution. Because the original hemorrhage is often of obscure etiology, it is usually considered to be "spontaneous."[7] The true nature of the problem seemed to be recognized first by Robinson in 1932, who reviewed the literature up to his time and pointed out the pertinent fact that the hemorrhages of this type were sometimes "encapsulated."[5]

The curability of such lesions by surgical measures had meanwhile been pointed out by Naffziger and Jones,[6] and subsequently demonstrated by de Lauwereyns [8] and Craig and Adson.[7] Subsequent investigators have limited and clarified the term, reviewed the interval literature, and pointed out that, although the interval between the onset of symptoms and the hemorrhage is usually short, it may be quite extended.[9] Others (Furlow et al.,[10] Pilcher,[11] Klemme [12]) have reported significant series of illustrative cases. In one series, of 16 cases, described by Hamby,[13] the wide range of possible causes, including even primary and metastatic lesions, was indicated.* That intracerebral "hematomas" may occur in missile wounds of the brain,[17] even as a result of explosions,[18] as well as in case of "blunt" injuries,[19] is also noteworthy.

* It is quite likely that some examples of presumed "spontaneous" intracerebral hemorrhage are actually instances of hemorrhage into a tumor, as Hamby [13] has pointed out. This presumption is also indicated in the case reported by Andre-Thomas, Schaeffer, de Martel, and Guillaume,[14] even though the patient was still living after two months. This was possibly true in one of the cases (Case 3) reported by Craig and Adson.[7] This possible error is pointed up in the case reported by Laruelle and Massion-Verniory,[15] in which the lesion ultimately proved to be a malignant glioma.[16] The recommendation of Furlow et al.[10] that biopsy of the wall of the cyst should always be done to rule out a neoplasm seems to be a wise one in view of this situation.

In the many contributions to the subject of intracerebral "hematoma," relatively little attention has thus far been given to its pathology and pathogenesis. As a basis for discussion, it is worth while to record the findings in a classical example of this lesion verified at autopsy.

Report of a Case

Multiple injuries sustained by a Negro man when struck by an automobile. Shock. Impairment of respiratory and cardiac function after epidural block. Continued stupor. Death from bronchopneumonia two weeks after injury. Autopsy. No evidence of recent brain injury but disclosure of posthemorrhagic old cystic cavity (intracerebral "hematoma") in right external capsule.

A Negro man, aged 49, was admitted to Los Angeles County Hospital on Nov. 15, 1951, in a state of shock. He had been struck down by an automobile while crossing the street, sustaining a compound fracture of the distal end of the left tibia and fibula and a comminuted supracondylar fracture of the right femur and proximal end of the fibula and soft-tissue injuries of both lower extremities. The patient was taken to surgery, where a débridement was done under cyclopropane-oxygen-thiopental (Pentothal) anesthesia. Four days later (Nov. 19) an attempt was made to do an epidural block (2% tetracaine [Pontocaine] hydrochloride), a procedure followed within a few minutes by temporary depression of both respiratory and cardiac function. The patient failed to regain consciousness but remained in stupor for the remaining nine days of life. He died on Nov. 28, of bronchopneumonia.

An autopsy was performed by Dr. Frederick D. Newbarr, of the Coroner's Office, who forwarded the brain to the Cajal Laboratory for study because of the possibility of cerebral anoxia incident to shock and of fat embolism. The cerebral arteries forming the circle of Willis and their afferents showed an advanced degree of atherosclerosis. The leptomeninges were somewhat opaque and the frontal convolutions slightly atrophic.

Coronal sections of the brain disclosed a fairly smooth-walled, rounded cavitation in the external capsule of the right cerebral hemisphere (Fig. 2). It extended from a level of the tips of the anterior horns of the lateral ventricles almost to the level of the splenium of the corpus callosum. It was filled with clear fluid of faint yellowish coloration. The cavity measured 3.4 by 1.4 cm. in its greatest sectional diameters. The lining of this cyst presented a brownish discoloration, sug-

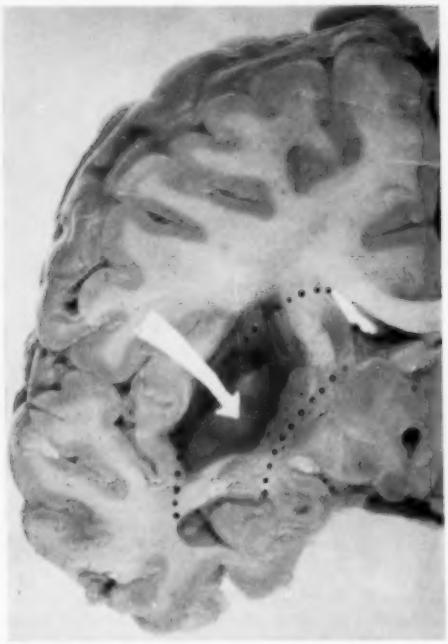


Fig. 2.—Intracerebral hematoma in form of a distended cyst. For a considerable interval wall of hematogenous cyst and ependyma of inferior horn and body of lateral ventricle (arrow) are in close apposition.

gesting its origin in a previous hemorrhagic effusion.

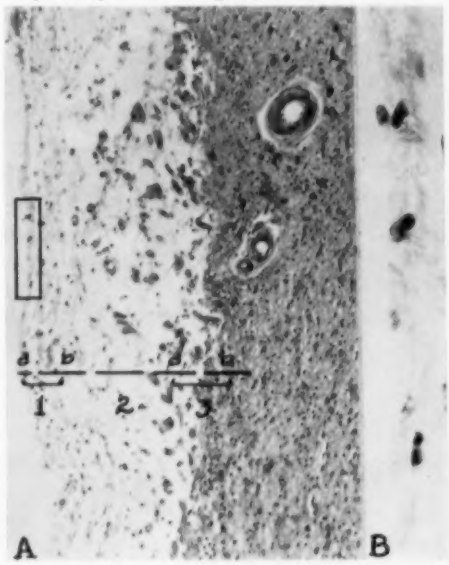
The remains of the white fibers in the external capsule were reduced to a thin band. The lenticular nucleus and thalamus were also considerably compressed by the cyst. The internal capsule was also considerably narrowed by its enlargement. Sections through the parieto-occipital regions of both hemispheres, the brain stem, and the cerebellum disclosed no additional lesions.

Blocks of tissue were taken from various areas of the cortex and the wall of the cyst in the right external capsule. The cortical sections showed a fibrous thickening of the leptomeninges, a patchy loss of the pyramidal nerve cells, and severe changes in many of the elements of this type that still remained. These changes, together with a marked proliferation of the capillary endothelium, suggested the occurrence of a severe degree of cerebral anoxia incident to shock, leading to an impairment of respiratory and cardiac function following epidural block.

Of more specific interest was the histological characteristic of the cyst lining. This lining varied considerably in thickness from one point to another. Three distinct layers in its structure could be made out: (1) the lining proper, made up of (*a*) a thin pseudoepithelial membrane composed of a single layer of elongated cells with one or more round or oval nuclei, and (*b*) a supporting layer of connective tissue, and (*2*) an irregularly broken intervening cleft which separated the "capsule" from (*3*) an underlying layer of combined connective tissue-glial reaction bordering the adjacent nervous tissues (Fig. 3). In this zone were to be seen scattered compound granular corpuscles laden with dark-brown hematogenous pigment (Fig. 4). This pigment was apparently the only residual of the once fairly large effusion of blood.

The lining membrane, or "capsule," of the cyst was in some regions thrown into shallow wrinkles, presumably because of the partially collapsed state of the cyst. The membrane was not unlike that of the internal, or arachnoidal, surface of a subdural hematoma. It was supported by a layer of loosely arranged connective tissue fibers, composed of both collagen and reticulin elements. This layer was almost entirely avascular. The individual reticulin fibers often presented a peculiar "feathered" appearance, resembling Spanish moss. The collagen fibrils were wavy in contour and arranged in strands parallel to the lining of the cyst (Figs. 5 and 6).

Fig. 3.—*A*, section through wall of hematoma, showing its individual layers. *1*, lining membrane of hematoma with (*a*) pseudoepithelial lining and (*b*) connective tissue reinforcement; *2*, intervening line of cleavage; *3*, zone of reaction of regional nervous tissues with (*a*) connective tissue reaction and (*b*) stratum of glial response. Hematoxylin and eosin; × 70. Inset *B* shows character of pseudoepithelial lining. × 350.



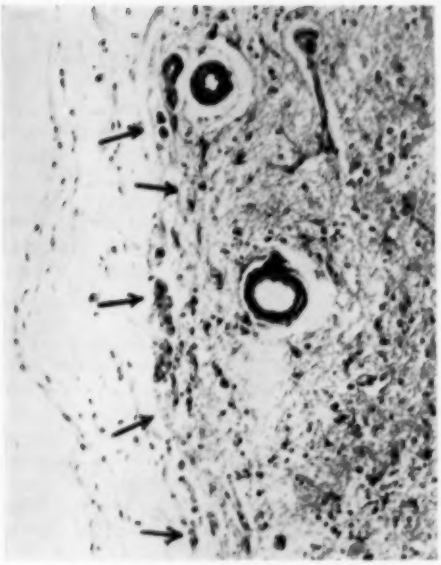


Fig. 4.—Section through wall of hematoma at greater magnification, showing pigment-laden macrophages (arrows) along border of residual nervous tissues. Hematoxylin and eosin; × 160.

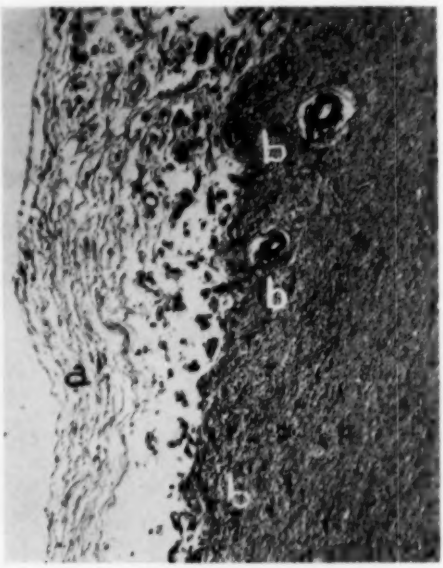


Fig. 5.—Collagenous response entering into formation of "capsule" (*a*). Dark border (*b*) along nervous tissue represents zone of glial fibrils, often found collected into bundles. Phosphotungstic acid-hematoxylin; × 70.

Fig. 6.—Same area with section impregnated with silver (Perdrau method), showing reticulin in "capsule" (*a*) and along border of nervous tissue (*b*). Mild vascular response along this border is also indicated (*c*). × 70.

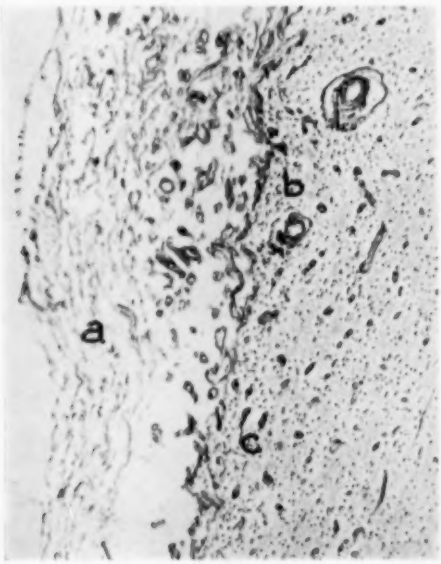
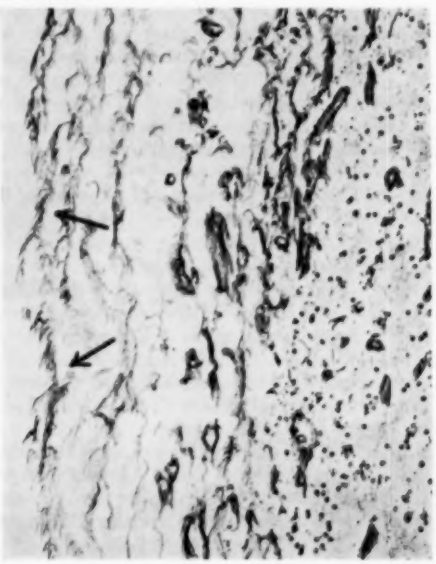


Fig. 7.—Detail of reticulin response in "capsule" shown with higher magnification. "Feathering" of reticulin fibrils is clearly shown. Perdrau, stain; × 160.

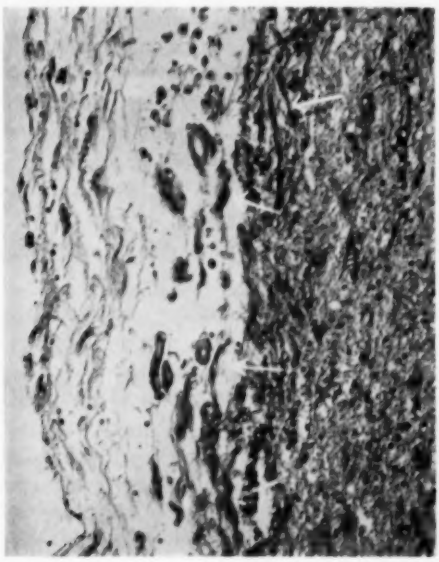


The very well-defined, though frequently interrupted, cleft (Fig. 3) could be traced in all sections and explained why such a lining membrane can be so readily detached at operation.

Bordering the subjacent nervous structures was another loose connective tissue layer, mingled with thin cords or strands of glial tissue, which extended out into a loose stroma like tufts of grass. This zone was also made up of an irregular net of collagen and reticulin fibers in which occasional small, well-formed blood vessels could be seen. There seemed to be a moderate increase in number of capillaries in the regional nervous tissues (Fig. 6).

The crenated margin of nervous tissues was marked by an irregular, broken line of pigment-laden phagocytes, which showed some predilection for the regional blood vessels. The larger vessels in this zone at times showed some thickening and early hyalinization, very likely a preexisting constitutional effect, not a local response to the hemorrhage. Special stains indicated that both reticulin (Fig. 7) and collagen fibers (Fig. 8) entered into the formation of the condensed border tissues, as well as the loose external stroma. But perhaps the most important constituents of this condensed zone were the glial fibrillae, usually arranged in sheaf-like bundles (Fig. 8). These bundles varied in size and number from one location to another. Oddly enough, there was only a minimal degree of glial proliferation.

Fig. 8.—Detail of collagen and glial response under same magnification for comparison. Arrows point to bundles of glial fibrils. Phosphotungstic acid-hematoxylin; × 160.



The fibers of the external capsule which lay against the hematoma were partially degenerated. In another area, some of the large cells of the putamen were also damaged.

Comment.—In this instance it was quite obvious that the cystic space was not related to the recent injury, certainly not to the even more recent cerebral anoxia. The brownish coloration noted in the lining of the cyst, moreover, indicated a hemorrhagic ancestry. Unfortunately, the patient's condition at the time of admission to the hospital precluded an adequate history of his previous medical condition, particularly of the "stroke" responsible for its genesis. Every effort made to contact friends or relatives has failed to give any information regarding his clinical condition prior to his fatal accident.

Pathology of Intracerebral Hematoma

A survey of the data now available in the numerous case reports of this lesion makes it possible to evaluate its essential pathology. The most important features which need specific elaboration are its precise location within the cerebral hemispheres, the accompanying changes in the regional cerebral cortex, its depth below the cortex, its size, the nature of its contents, the character of the cyst wall, and its relation to the lateral ventricle. The location of this group of focal cerebral hemorrhages is probably quite significant. A survey of reported cases indicates that these hemorrhages are located most frequently in the occipital, the parietal, the temporal, or the frontal lobe. Only rarely are they found in the central (or ganglionic) region. The reason for this tendency toward distal subcortical localization explains the fact that such effusions are less often fatal than are ganglionic ones.

Changes in the overlying cortex are usually evident at operation in the form of convolutional flattening, and at times of bluish coloration if the effusion is relatively superficial. Actual subarachnoid hemorrhage or yellow-brown pigmentation may

also be found in this region. Incision or a needle puncture through a flattened convolution will disclose the exact depth of the lesion. It is seldom very deep, usually being reported as 1 to 3 cm. below the cortex. When the extravasation is reached, the character of the contained fluid will be found to vary considerably from one case to another. In recent effusions the clot may be quite solid, lying within a well-defined cavity. In other cases small clots are found suspended in liquid blood or bloody fluid. In still older lesions the liquid may be brown or greenish in color. The older the lesion the lighter in color and more fluid the content of the cyst, until ultimately only a clear, watery fluid remains.

When the cavity is emptied of its contents, it is usually found to be relatively small. In surgically verified cases, the cysts are commonly estimated to be 3 to 3.5 cm. in diameter, which probably represents its size after contracture. The character of the cyst lining varies with age. Ragged in case of recent effusion, the cyst wall becomes smoother as time goes on. Ultimately, the cavity appears to be lined by a thin, translucent membrane. This lining, moreover, is separable and can be readily peeled away from the wall of the cavity.

Sections of the lining membranes from enough cases have become available for histological study to indicate that the tissue reaction to intracerebral hemorrhage is by no means invariably the same. Yet in its essential characteristics the lining membrane is quite uniform in structure. This membrane, or "capsule," is usually considered to be made up of flattened glial elements which come to resemble epithelial cells. In this lining membrane, connective tissue elements in the form of both collagen and reticulin fibers can also be demonstrated. This capsule is only feebly attached to the underlying nervous tissues by a loose scar of combined connective tissue-glial origin. The presence of an extensive, though interrupted, cleft explains why this membrane can be so readily detached. In recent cases pigment-laden macrophages may be found within it. For the most part, however, pigment is more abundant in the deeper tissues, probably residuals of focal hemorrhages in the loose tissues about the original clot.

The regional tissues undergo variable degrees of softening, endothelial proliferation and new-blood-vessel formation (Robinson[5]), connective tissue reaction (Bagley[20]), and calcareous deposition (Pilcher[11]). The last process may be so extensive as to produce a calcareous shell about the cyst.[21] The degree and nature of connective reaction apparently varies remarkably from one case to another. In some cases this reaction consists of a reticulin proliferation; in others, an increase in collagenous elements, possibly even of elastic connective tissue. The thickness of this layer of connective tissue reaction also varies, at times being associated with local extensions into regional tissue.[11]

Because in most instances the lesion has been identified at operation, the exact relation of the cyst cavity to the corresponding horn of the lateral ventricles is usually not clear. In some instances, however, where an air study has been done, a small communication between the cyst and the ventricle has been demonstrated. In the occasional case in which the cyst was demonstrated at autopsy, its proximity to the ventricle has been mentioned but not particularly stressed.

Pathogenesis of Intracerebral Hematoma

It has long been recognized that two possible reactions may take place in response to a nonfatal intracerebral hemorrhage. In the usual case, there is a progressive deterioration in the relatively "dry" blood clot. There is a corresponding shrinkage in the artificial cavity hollowed out by the original effusion. The lesion is ultimately reduced to a mere slit in the tissues, whose border may remain deeply stained for some time

with hematogenous pigment. Microscopically, this border is found to be composed of a loose glial scar, in which numerous pigment-laden phagocytes are found. In the second type of lesion, the cavity is filled with blood fluid in which clots are suspended. If the patient survives for a sufficiently long time, the solid portions of the clot undergo dissolution, leaving only a distended, sharply delineated, fluid-filled cavity. This reaction is obviously not dependent upon the inherent nature of the hemorrhagic effusion, for this factor always remains the same. What, then, is the essential difference in the development of the two lesions?

Hamby [13] has concluded that the presence of a fluid-filled sac within the substance of the brain implies a similarity to subdural hematoma, with encapsulation and subsequent liquefaction of the clot. This concept was supported by the occurrence of a "capsule" lining the hemorrhagic cavity, as reported by several students of the problem (Douglas,[22] Craig and Adson,[7] Pilcher,[11] and Hamby [13]). Rowbotham and Ogilvie [23] carried this concept of similarity a step further by suggesting that the fluid in the hemorrhagic cavity is derived from the surrounding tissues, resulting thereby in a "blood cyst" of increasing size. If this is the case, why does not an intracerebral hematoma develop in every instance of nonfatal hemorrhage?

The answer seems clear enough, since it is supported by certain facts, as furnished in previous studies and amply demonstrated by the case here described. The localization of clear-cut examples of intracerebral "hematomas" adjacent to one of the horns of the lateral ventricles and the actual demonstration of small communications between the hemorrhagic cavity and the ventricles, either by air study (Furlow et al.[10]) or by autopsy, point to the ventricles rather than to adjacent nervous tissues as the source of the fluid. In the case reported herewith, the close proximity of the cyst to the ventricle, being separated only by the lining membrane and the ependyma, further supports this conclusion.

There remains only one question to be answered. What part does the lining "capsule" play in the process of transfer of fluid from the ventricle to the cystic cavity? It would appear that this membrane does not always act as a semipermeable membrane under these circumstances, as in the case of chronic subdural hematoma. This is suggested in cases in which a direct communication exists between the ventricle and the cavity (Furlow et al.[10]).† But even when no such atrium is demonstrated, as in the example reported herewith, the behavior of the ependymal lining in the process of transference of fluid from the ventricle into the cyst must also be considered. In this situation, the combination of a somewhat attenuated ependyma (incident to a dilated ventricle) and whatever "capsule" may have formed apparently must act in conjunction as a semipermeable membrane for the passage of fluid into the original hemorrhagic cavity.

Summary and Conclusions

As a relatively rare consequence of hemorrhage, either traumatic or spontaneous, into the cerebral centrum, a syndrome of increasing intracranial pressure may develop. The attendant symptoms often suggest those incident to an intracranial tumor. The location of such hemorrhages in the vicinity of one of the horns of the lateral ventricle, and, at times, the actual demonstration of a communication between the blood cyst and the ventricles suggest that the progressive enlargement of this cyst is the result of transference of fluid from the ventricles, and not its absorption from

† Such communications may be artifacts incident to air study. If constant, why should not the cyst drain more or less continuously into the ventricle and finally collapse after the clot had disappeared? On the other hand, one such case (Case 4 of Furlow et al.[10]) suggests that the drainage of such blood into the ventricular system may have been the cause of the obstructive hydrocephalus incident to adhesions about the exits of the fourth ventricle.

the surrounding tissues, as some have supposed. This conclusion is supported by the fact that relatively few nonfatal hemorrhages into the cerebral centrum result in the formation of such a "hematoma." The increasing size of this lesion usually demands surgical intervention. It is for this group of progressively expanding posthemorrhagic cysts that the term "intracerebral hematoma" should be reserved.

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Cranial Nerve Syndromes Associated with Nasopharyngeal Malignancy

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Neurologic syndromes limited to cranial nerve involvement are infrequent and may offer diagnostic difficulty. The possibility of a neoplastic process as the etiologic factor requires serious consideration. Nasopharyngeal malignancy in particular, as Woltman [1] has pointed out, tends to implicate structures at the base of the skull. He demonstrated cranial nerve palsies in 25 of a group of 118 patients with neoplasia in this area. In 15 the neurologic manifestations preceded other signs. New [2] found cranial nerve complications in 31% of his series of 194 cases. Signs referable to the primary site of these tumors are often inconspicuous or absent. Thompson and Grimes [3] state that nasal obstruction, discharge, or epistaxis occurs early in less than 30%. Since these patients frequently first seek medical advice because of their neurologic disability, it is important that the neurologist be aware of the cranial nerve complications of malignancy in the nasopharynx. The primary tumor, while surgically inaccessible, may be controlled by irradiation if recognized early. We therefore report 11 cases, in 8 of which necropsy was performed.

Report of Cases

CASE 1.—A white man, aged 50, complained of double vision, vertigo, and unsteady gait. Neurologic examination revealed only a left external rectus muscle paralysis. There was spontaneous improvement for several weeks, but overnight the patient became completely deaf in the right ear and developed a right sixth nerve palsy. At this time the disk margins appeared blurred. Four months later a right peripheral facial palsy was noted. A roentgenogram of the skull was negative. Exploratory craniotomy revealed no space-taking lesion. The patient died six months after the onset of symptoms.

At necropsy, necrotic tumor tissue was found in the nasopharynx. The base of the skull was intact, and no obvious neoplastic invasion of intracranial structures was observed. Histologic study of the tissue around the left cavernous sinus, however, demonstrated infiltration of the dura over the Gasserian ganglion with malignant cells of the lymphoma type. Tumor cells had invaded the perineurial sheath of the ganglion (Fig. 1) and its roots and were present in the adventitia of the adjacent internal carotid artery as it emerged from the carotid canal and in the capsule of the pituitary gland. Extensive infiltration of the subarachnoid space was present over the brain stem, cerebellum, and basal surface of the cerebrum (Fig. 2). No actual tumor nodules occurred in this location. Neoplastic cells were diffusely scattered in a mesh of collagenous fibers and entangled in the adventitia of the subarachnoid vessels. No particular localization around cranial nerve fibers was observed, but neoplastic infiltration was dense around the optic chiasm and along the optic nerves. Within the optic sheath, the subarachnoid space was blocked by tumor cells, which invaded the nerve along connective tissue trabeculae (Fig. 3). No distant metastases were found.

CASE 2.—A Negro man, aged 57, noted a peripheral facial palsy and anesthesia of the right side of the face six years before death. One year after onset severe pain developed in the same area. At this time exploratory craniotomy was done with section of the trigeminal nerve for relief of pain. One year after this operation the patient became deaf in the right ear and developed dim vision in the right eye and ptosis of the right eyelid. During the next three years he became progressively blind in both eyes and developed deafness and tinnitus on the left, with unsteady gait, difficulty in articulation, and regurgitation of liquids through the

Received for publication March 3, 1956.
From the Philadelphia General Hospital.
Read in part at the joint meeting of the Philadelphia-Baltimore and Washington Neurological Societies, November, 1954.
† Dr. Yaskin died Aug. 10, 1955.

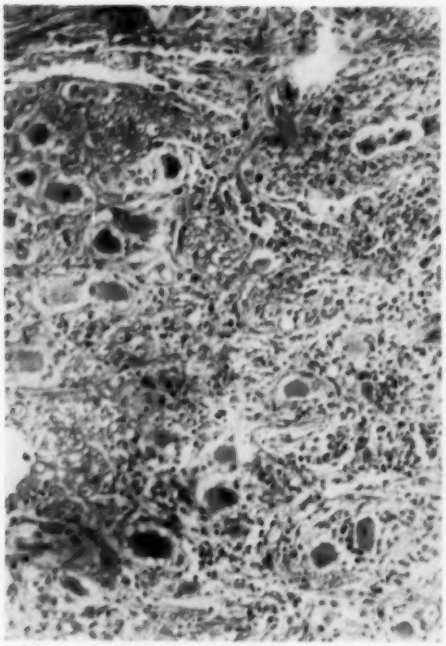


Fig. 1 (Case 1).—Photomicrograph showing neoplastic invasion of Gasserian ganglion by tumor cells. Reduced to 59% of mag. × 92.

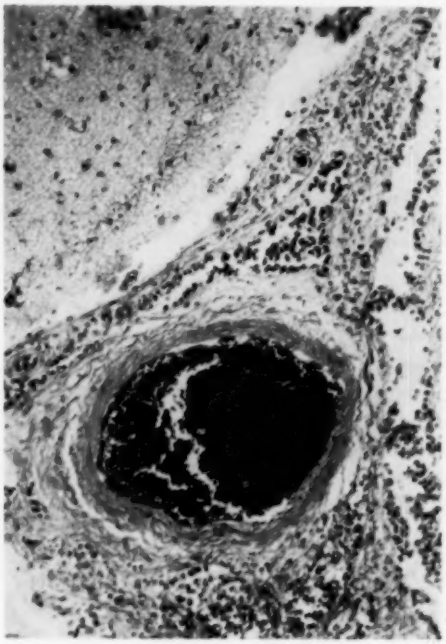
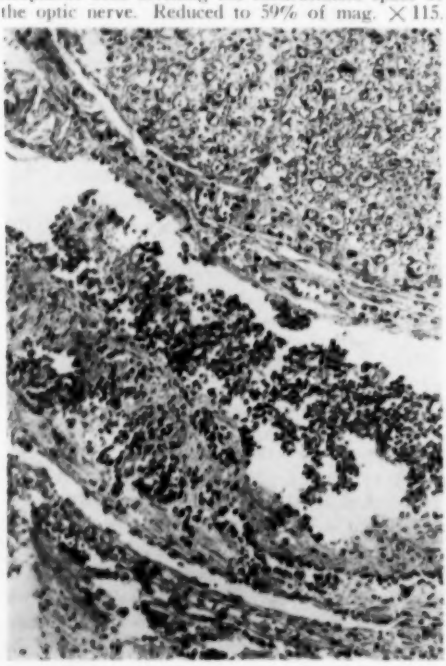


Fig. 2 (Case 1).—Photomicrograph showing neoplastic invasion of the subarachnoid space of the cerebral hemispheres by tumor cells. Reduced to 59% of mag. × 102.

Fig. 3 (Case 1).—Photomicrograph showing neoplastic cells blocking the subarachnoid space of the optic nerve. Reduced to 59% of mag. × 115.



nose. Before death, a bilateral Babinski sign with generalized hyperreflexia was noted.

At necropsy, neoplastic tissue (epidermoid carcinoma) was found in the nasopharynx. Structures at the base of the brain were engulfed by a sheet of dense white neoplastic tissue, which filled the interpeduncular space and spread over the optic nerves and chiasm (Fig. 4). The mass was continuous through the tentorium into the posterior fossa, where it compressed the right lateral surface of the pons and extended across to fill the left cerebellopontile angle (Fig. 5). In this location the seventh and eighth nerves were incorporated into the tumor (Fig. 6). The neoplastic tissue was firmly fixed to the dura but had not invaded the extradural space or the underlying bone. Neoplastic cells had invaded the subarachnoid space and the choroid plexus at the foramen of Luschka (Fig. 7). The subdural channels along both optic nerves were obliterated. Infiltration of the capsule of the pituitary had occurred without actual invasion of the gland. Metastatic lesions were present in the lung.

Case 3.—A white man, aged 31, first noted a painless, rapidly growing mass on the left side of the neck, which disappeared following irradiation. Two weeks after the last x-ray treatment, he suddenly became blind in the left eye and developed

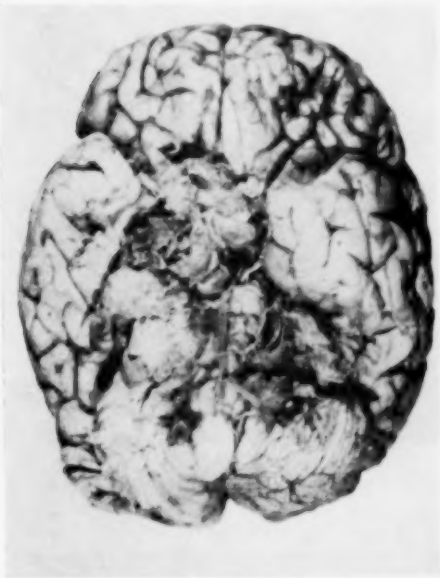


Fig. 4 (Case 2).—Gross specimen showing intracranial invasion primarily in the subdural space. The dura has been stripped by blunt dissection to show obliteration of basal structures. Tumor tissue has invaded the posterior fossa and filled both cerebellopontile angles.

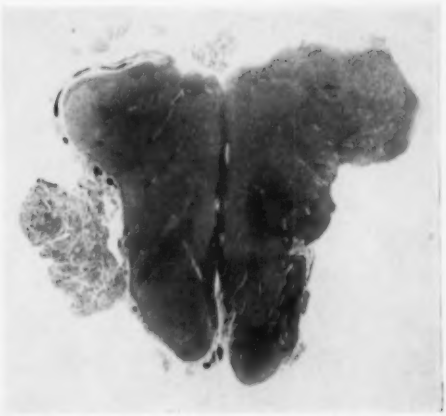


Fig. 5 (Case 2).—Photomicrograph of pons in cross section showing tumor in cerebellopontile angle which has invaded along the extramedullary course of the eighth nerve. Reduced to 59% of mag. ×4.

ptosis on the same side. Pain in the left ear and numbness of the left side of the face rapidly followed. Four months later the growth in the neck recurred. Examination revealed a dilated and fixed pupil on the left with limitation of all movement of the eyeball and lid ptosis. Anesthesia of the right side of the face was present, with hypesthesia on the left. There was left peripheral facial palsy with weakness of the right side of the face, paralysis of the soft palate on the left; and difficulty in swallowing. The patient died six months after the initial symptoms.

At necropsy, neoplastic tissue (lymphoma) was found filling the nasopharynx. The basal dura was intact, but the floor of the middle fossae was shallow and there was obliteration of the sella turcica. On stripping the dura, the entire bony structure, including the sella, was found to be replaced by neoplastic tissue. Both cavernous sinuses were obliterated by the mass, and the left carotid artery and Gasserian ganglion were incarcerated in tumor tissue. Neoplastic cells had invaded the ganglion and extended along the root of

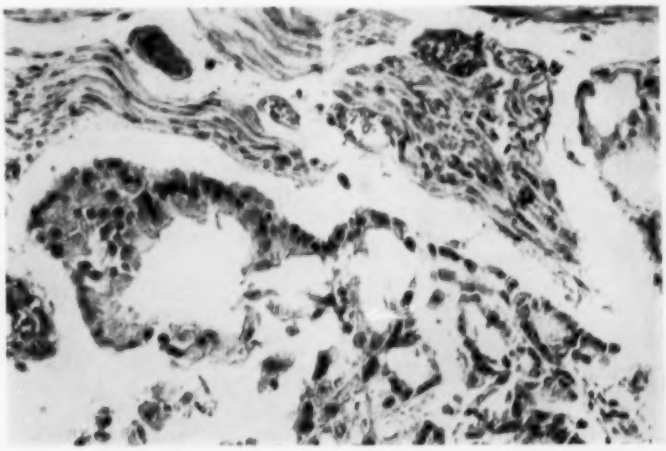


Fig. 6 (Case 2).—Photomicrograph showing nerve roots incarcerated within tumor mass. The nerves are not actually invaded but have degenerated as a result of compression. Reduced to 61% of mag. ×90.

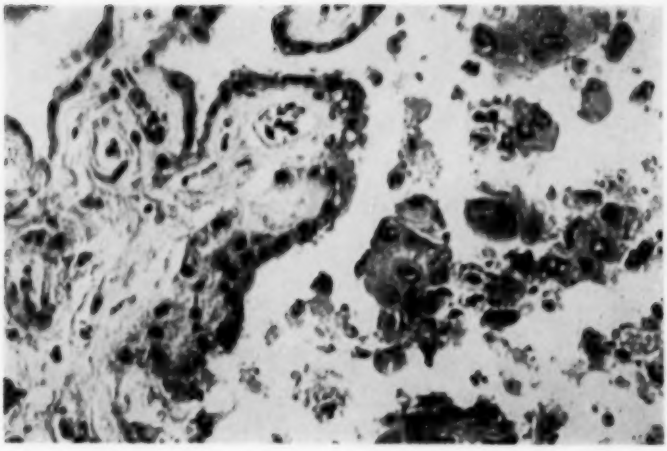


Fig. 7 (Case 2).—Photomicrograph showing tumor cells within the choroid plexus at the foramen of Luschka. Reduced to 61% of mag. × 137.

the nerve into the subarachnoid space. Superficial invasion of brain tissue had occurred at the temporal poles and along the infundibular stalk. Metastatic tumor was present in the lung and pancreas, as well as the cervical lymph nodes.

Case 4.—A white man, aged 52, was admitted because of epileptiform seizures which had occurred at irregular intervals for one year. On examination, he was found to have a painless mass in the left side of the neck, which on excision was found to be malignant (metastatic undifferentiated carcinoma). He was free of seizures for six months but then developed a left external rectus palsy, followed rapidly by a peripheral facial palsy, deafness, and weakness of the soft palate, all on the same side. Speech became nasal. Irradiation was instituted, with some regression of the neurologic signs. Two years after his initial symptom, however, he developed acute meningitis and died.

At necropsy, no neoplastic tissue could be identified in the nasopharynx. The patient, however, had been subjected to intensive irradiation during the last six months of life. Extensive purulent exudate filled the basal cisterns of the brain and extended over the convexity of the hemispheres. There was erosion of the dura in the left posterior fossa, extending from the internal auditory meatus to the foramen magnum. The petrous bone beneath was necrotic and histologically diffusely infiltrated with malignant undifferentiated tumor cells, similar to those present in the cervical lymph nodes. No neoplastic involvement of the middle fossa could be demonstrated. No distant metastases were present.

Case 5.—A Negro man, aged 43, first complained of difficulty in chewing on the left, numbness of the same side of the face, and deafness and tinnitus in the left ear, all of which developed over a period of several weeks. On examination, a left sixth nerve palsy and a left peripheral type of facial weakness were also found. A large, painless mass was noted on the left side of the neck, which the patient stated had been present for one year. A history of nasal discharge and repeated epistaxis over the same period was obtained. Examination revealed a tumor in the nasopharynx. Biopsy of the mass in the neck was reported as showing metastatic malignancy. X-ray therapy was instituted, with some relief of cranial nerve symptoms, but the patient developed uncontrollable nasal hemorrhage and died 18 months after the appearance of the mass in the neck.

Necropsy revealed that neoplastic tissue (undifferentiated carcinoma) filled the nasopharynx and extended into the left antrum. The dura over the base of the skull was intact. Osteolytic changes, however, had occurred in the floor of the sella and extended through the dorsum to involve the basilar portion of the occipital bone. Similar alterations were present in the left petrous apex and adjacent sphenoid bone. Examination of tissue from the region of the left Gasserian ganglion demonstrated neoplastic involvement of the dural sheath and invasion of the ganglion. No distant metastases were found.

Case 6.—A white man, aged 50, developed a mass on the right side of the neck, which had been reported as a metastatic malignancy. Eleven months later he experienced intractable pain in the neck and over the left eye. Shortly thereafter ptosis of the left lid was observed. Two months later bilateral sixth nerve palsy was present. Skull roentgenography early in the course was negative, but later showed destruction in the region of the middle fossa. The patient died 31 months after the development of the mass in the neck.

At necropsy, neoplastic tissue (lymphoma) was identified in the nasopharynx. The bone and dura of the floor of the middle fossae were replaced by neoplastic tissue. Tumor had completely destroyed the sella and extended through the basilar portion of the occipital bone to erode the anterior lip of the foramen magnum. Tumor tissue in the posterior fossa compressed the ventral surface of the pons and the basilar artery and partially obstructed the foramen magnum. The Gasserian ganglia were embedded in tumor, and neoplastic tissue obliterated the subdural space of both optic nerves. Metastatic nodules were present in the vault of the skull, the bodies of the lumbar vertebrae, and the liver.

Case 7.—A white man, aged 36, developed a painless growth on the left side of the neck. A diagnosis of metastatic malignancy of the lymphoma type was made on biopsy and the nasopharynx suggested as its origin. Intensive irradiation was given, but eight months later the patient showed paralysis of the left external rectus and corneal anesthesia was present bilaterally. Ten months after appearance of these symptoms intractable pain began in the left side of the face, for which two intracranial operations were performed, without relief. Complete left ophthalmoplegia developed. An exploratory frontoparietal craniotomy at this time disclosed no intracranial mass lesion. The patient developed a left peripheral facial palsy. Terminally, there were deviation of the tongue to the left and paralysis of the soft palate on the left. Death from meningitis occurred two years after the onset of symptoms.

Necropsy studies in this case were complicated by the extensive surgical procedures, terminal infection, and tissue necrosis. The nasopharynx was filled with necrotic tumor tissue. A mass of necrotic material filled the left middle fossa, replacing the floor and dorsum of the sella, the tip of the petrous bone, and the adjacent sphenoid bone. Necrotic tumor tissue obliterated the cavernous sinus on this side and constricted the internal carotid. The greater part of the Gasserian ganglion had been surgically removed. Extensive plastic exudate filled the basal cisterns. No visceral metastases were present.

Case 8.—A white man, aged 58, noted pain in the left side of the face, followed by drooping of the left eyelid, and vertigo. Five months later examination showed a complete left third nerve paralysis, hypesthesia of the right side of the face, right corneal anesthesia, and weakness of the right masseter. Weakness of the right half of the soft palate was also present. Painless enlargement of the nodes of the neck was noted bilaterally, biopsy of which showed metastatic epidermoid carcinoma. Destruction of the right petrous pyramid and of the right side of the sella was demonstrated by roentgenogram. Irradiation therapy was given, but six months later left external rectus paralysis developed and hearing was greatly diminished in both ears. Progression in destruction of the floor of the skull was demonstrated by roentgenogram. The patient was subjected to a prefrontal lobotomy for relief of pain and died two days later, 10 months after the onset of symptoms.

Postmortem examination was performed at the Hospital of the Graduate School of Medicine of the University of Pennsylvania. Necrotic tumor tissue (epidermoid carcinoma) was found in the nasopharynx. Neoplastic tissue replaced the floor and basal dura of the right middle fossa, with destruction of the right side of the sella turcica, the petrous apex, and the adjacent sphenoid bone. The cavernous sinus and the Gasserian ganglion were obliterated by neoplasm. No distant metastases were found.

Case 9.—A white man, aged 34, had noted pain and fullness in the throat for three months. He then developed severe, constant pain in the right side of the face. When he was seen seven months after the onset of symptoms, a partial peripheral facial palsy, weakness of the soft palate, and decreased hearing on the right were present. Weakness of the right sternocleidomastoid muscle was also noted. Metastases to the nodes of the neck were present, and a roentgenogram of the skull demonstrated destruction of the right middle fossa. Tumor was present in the nasopharynx, biopsy of which was reported as showing lymphoma. Under irradiation there was amelioration of the neurologic condition, but death from pneumonia occurred 29 months after the initial symptoms. Autopsy was not obtained.

Case 10.—A white man, aged 48, noted a sudden onset of tinnitus in the right ear, followed two days later by complete deafness. When he was seen three months later, anesthesia of the right side of the face was present, with masseter weakness on the same side and paralysis of the right external rectus. Weakness of the right half of the soft palate and deviation of the tongue were also noted. No erosion of the skull was noted on roentgenogram. Tumor, which was reported as epidermoid carcinoma, was present in the nasopharynx. Deep x-ray therapy was initiated, but the patient died nine months after the onset of symptoms. Autopsy was not obtained.

Case 11.—A white man, aged 43, was first seen because of paralysis of the right sixth nerve. For six months prior to the onset of the cranial nerve palsy he had noted fullness and pain in the throat. A discharge from the right ear had been present

TABLE 1.—*Clinical and Pathologic Features*

Case, No.	Age, Yr.	Sex	Duration of Illness	Initial Complaint	Cranial Nerve Involvement	Symptoms Primary Site	Regional Metastasis	Skull Erosion	Intracranial Extension	Distant Metastasis
1	50	M	6 mo.	Diplopia; vertigo	R. 7, 8 Bilat. 2, 6	–	–	–	Subarachnoid; optic N.	–
2	57	M	6 yr.	Anesthesia; palsy (R) face	R. 3, 5 (s) 7 Bilat. 2, 8, 9, 10	–	Cervical nodes	–	Subdural, subarachnoid, parenchymal	Lung
3	31	M	6 mo.	Mass in neck	L. 2, 3, 4, 6 Bilat. 5 (s) 7, 9, 10	–	Cervical nodes	+	Subdural, subarachnoid, parenchymal	Lung; pancreas
4	52	M	2 yr.	Seizures; mass in neck	L. 6, 7, 8, 9, 10	–	Cervical nodes	+	Subarachnoid	–
5	43	M	1½ yr.	Difficulty in chewing; numbness of left face	L. 5 (m. s.) 6, 7, 8	Nasal discharge; epistaxis	Cervical nodes	+	Subarachnoid	–
6	50	M	2½ yr.	Mass in neck	L. 3, 5 (s) Bilat. 6	–	Cervical nodes	+	Subdural	Vault skull; vertebrae; liver
7	36	M	2 yr.	Mass in neck	L. 3, 4, 6, 7, 9, 10, 12 Bilat. 5 (s)	–	Cervical nodes	+	Subdural	–
8	58	M	10 mo.	Pain (L) face; ptosis (L)	R. 5 (m) 9, 10 L. 3, 6 Bilat. 5 (s), 8	–	Cervical nodes	+	Subdural	–
9	34	M	2½ yr.	Pain, fullness of throat	R. 5 (s) 7, 8, 9	Pain, fullness of throat	Cervical nodes	+ (x-ray)	No necropsy	
10	48	M	9 mo.	Deafness; tinnitus (R)	R. 5 (s, m) 6, 8, 9, 10, 12	–	–	– (x-ray)	No necropsy	
11	43	M		Pain in throat	R. 6	Pain in throat	–	– (x-ray)	Asymptomatic 8 mo. after irradiation therapy	

TABLE 2.—*Cranial Nerve*

Cranial Nerve Involved			No. of Cases
II			3
	Papilledema	1	
	Blindness	2	
III, IV, VI			10
	Ptosis	2	
	Complete 3d nerve paralysis	1	
	Complete ophthalmoplegia	2	
	External rectus paralysis	7	
V			8
	Sensory (pain and/or numbness of face)	5	
	Sensory and motor	3	
VII	Peripheral facial palsy		7
VIII			7
	Cochlear	4	
	Cochlear and vestibular	3	
IX-X			7
	Palatal weakness	7	
	Dysarthria	1	
	Nasal voice	1	
	Difficulty swallowing	1	
XI	Sternocleidomastoid paralysis		1
XII	Deviation of tongue		2

for one month. Examination of the nasopharynx revealed a tumor mass, biopsy report on which was epidermoid carcinoma Grade 3. The skull roentgenogram was negative. Irradiation therapy was given. Examination eight months later showed regression of the tumor mass and restoration of function of the cranial nerve.

Clinical Features

The infrequent occurrence of these cases is demonstrated by the fact that the eight autopsied cases were found in a series of over 30,000 postmortem examinations.

All patients in this study were men ranging in age from 31 to 58 years. The predominance of men in cases of nasopharyngeal malignancy has been noted by other investigations; 80% of the cases reported by Martin and Blady [4] occurred in men. Except for a predilection to cranial nerve involvement, the neurologic syndromes presented were by no means stereotyped (Table 1.) The clinical picture was characterized by individual differences in the order and combination of cranial nerve palsies, as well as in the particular nerves affected (Table 2). Extraocular palsies were present in all but one patient at some time during the course, but the pattern was rarely duplicated. Pain or numbness of the face, diplopia due to external rectus weakness, and peripheral facial palsy were the most frequent complaints; these symptoms, however, rarely occurred simultaneously nor did the triad appear in its entirety in the same patient. The eighth nerve was also frequently implicated, either with sudden or progressive deafness and tinnitus or, less often, with vertigo, nausea, and incoordination. Involvement of the medullary cranial nerves was commonly observed late in the course but occasionally as a presenting symptom. Visual disturbances, progressing to complete blindness, were present in two cases, and blurring of disks occurred early in a third.

The course of cranial nerve damage was essentially progressive, but the period of evolution was subject to considerable variation. More than half of the group died within 10 months after the appearance of cranial nerve signs, and only one survived longer than 2 years. Unilateral disability was the rule at the onset, but during the course extension to the opposite side occurred in the majority. Initial damage was occasionally limited to a single nerve; more frequently, however, multiple involvement was present from the beginning or developed within a few weeks. Once established, the process might remain static for a considerable period, in one patient as long as a year. Transient, spontaneous remissions occurred in two patients. Inexorably, extension of the disease followed.

The march of cranial nerve palsies followed no predictable pattern and did not appear to depend upon anatomic contiguity. Despite the close anatomic proximity of the nerves in the middle fossa, fifth nerve damage and extraocular palsies were not always concurrent. In some instances trigeminal symptoms were absent or appeared at appreciable intervals before, or after, the ocular phenomena. In spite of the frequency of extraocular palsies, complete ophthalmoplegia developed in only two patients. More frequently, the third or the sixth nerve alone was involved. Rarely, particularly in the case of the third, fifth,

and eighth nerves, was an entire nerve distribution affected. Damage to the oculomotor nerve might initially be limited to the supply of the levator palpebrae and either show no further progress or become complete only after considerable time. Pain or numbness of the face, while an early and frequent complaint, rarely was associated with involvement of the motor division of the fifth nerve, although in one instance masseter weakness preceded sensory signs. Vestibular disturbances accompanied deafness in less than half the cases; in one, however, vertigo, nausea, and incoordination preceded loss of hearing.

Necropsy Observations and General Comment

The mechanism of cranial nerve palsies in nasopharyngeal malignancy is by no means conclusively established. Interpretation for the most part has been based upon anatomic considerations or clinical and radiological observations; relatively few necropsy studies, other than reports of isolated cases in the early literature, have been published. On the basis of the frequency of erosion of the base of the skull in this condition, Woltman [1] concluded that the nerves were involved extracranially. He considered intracranial extension was limited by the basal dura. Martin and Blady,[4] while subscribing to the extradural localization of intracranial growth, pointed out that nerve syndromes were frequently well established before damage to the skull could be demonstrated. In their opinion, extension from the primary site occurred directly into the subdural space by soft-tissue continuity through the foramen lacerum, with erosion of bone following, rather than initiating, intracranial invasion.

The progress of disease as disclosed at necropsy may, in some instances, be too far advanced to determine the origin of cranial nerve injury; the findings in our cases, however, suggest that identical mechanisms may not operate in all instances. 4, but actual destruction of cranial nerve foramina in the posterior fossa could be demonstrated. The skull, however, was com- Intracranial extension was absent in Case pletely intact in two patients, in one of whom cranial nerve palsies had been present for more than three years. Erosion was confined to the right middle fossa in Case 8, although initial nerve damage was on the left. The occurrence of neoplastic dissemination into the subarachnoid space in three cases in our group suggests that in some instances cranial nerves may be involved before penetrating the dura. Invasion of the meninges followed extension from the subdural space along the internal carotid artery in one case and along the fifth nerve in a second. Where extensive neoplastic tissue is present within the cranial cavity, such dissemination may merely represent terminal spread of uncontrolled growth. In Case 1, however, bone lesions were absent, and intracranial extension, other than to the subarachnoid space, was limited to microscopic invasion of structures around the foramen lacerum of one side. The bilateral palsies and the early choking of the optic disks in this patient point to primary involvement of the cranial nerves in their subarachnoid course.

The development of choked disk as a result of neoplastic obliteration of the subarachnoid space of the optic nerve is of some interest. Involvement of the optic nerve is not uncommon in nasopharyngeal malignancy and is usually attributed to compression by expansion of the growth within the orbit. Martin and Blady [4] considered that such invasion resulted from direct extension along the extradural course of the internal carotid artery through the superior orbital fissure. Three patients in this series presented visual impairment, and advanced optic atrophy was found at necropsy in a fourth. Intraorbital tumor tissue was not found in these cases; damage to the optic nerve had resulted from neoplastic obliteration of either the subdural or the subarachnoid channels of the nerve itself. Additional injury in one case (Case 3) resulted from compression of the distal portion of the

nerve and the chiasm by subdural tumor growth in the middle fossae.

These findings are at variance with the dictum that intracranial growth in nasopharyngeal malignancy is confined to the subdural space. Tumor was present within the cranial cavity in seven of the cases studied at necropsy, but in none was the process strictly confined to a subdural location. Neoplastic tissue in Case 2 formed a dense sheet entirely above the dura, intimately adherent to structures in the interpeduncular space and infiltrating through the tentorium into the posterior fossa. Elevation of the dura in instances where there has been extensive growth through bone has been considered proof that this membrane forms an effective barrier to further penetration. Neoplastic replacement of the base of the skull in three cases, however, had completely obliterated the dura in its upward extension into the middle fossa; in two, where the dura was elevated and seemingly intact, invasion of deeper structures could be demonstrated on microscopic study.

The nature and location of the pathological alterations of the skull merit mention. The term "erosion" has frequently been applied to the cranial lesions. While this may properly describe the radiological appearance, the condition present at necropsy could, in many instances, be more accurately designated as neoplastic replacement. The base of the skull in such cases was converted into a homogeneous sheet of tumor tissue, often 3 to 4 cm. in thickness, within which were embedded the neural and vascular structures of the extradural space. Earlier investigators have stressed invasion of bone in the region of the foramina of the floor of the middle fossa. Recently Rosenbaum and Seaman [5] have demonstrated by roentgenographic studies destruction of the floor and base of the dorsum of the sella turcica. Lesions of the skull at necropsy were frequently more extensive than suggested by previous reports. Erosion of the floor of the sella with destruction of the ipsilateral side of the entire dorsum was present in all cases in which the floor of the middle fossa was involved. Complete replacement of the sella turcica by tumor was observed in Case 6, where destruction of the base of both middle fossae had occurred. Invasion of the posterior fossa resulted in two cases, from extension of the neoplastic process through the dorsum sellae to the basilar portion of the occipital bone.

Although considerable attention has been paid to the diagnostic value of cranial extension in nasopharyngeal malignancy, the tendency of these tumors to metastasize early to the cervical lymph chains is also of clinical importance. Tumor masses were present in the neck in seven cases in our series and preceded cranial nerve palsies in 5 cases. Spread to the cervical nodes has been reported in 50% of all cases of malignancy in the nasopharynx. It was observed at the time of the first examination in 77% of the 87 patients studied by Martin and Blady [4] and in 5 of Woltman's [1] 25 cases with cranial nerve damage.

Metastasis to distant locations has been less well documented. Martin and Blady [4] state that systemic metastases are more frequent with cancer of the nasopharynx than with other growths of the upper respiratory and alimentary tracts. According to their observations, skeletal spread is most frequently found with liver and lung involvement in the late stages. Vertebral metastasis was observed in only one instance in Woltman's series. Three of the eight cases in our group in which necropsy was performed presented metastases to distant organs. These were limited to the lung in one case and to the lung and pancreas in a second, while in the third nodules were present in the vault of the skull, the lumbar vertebrae, and the liver.

Classification of the primary malignancy in the nasopharynx was not of primary interest in this study. No single type of neoplastic growth was present in all cases. Identification at necropsy was often difficult as a result of infection, necrosis, or antecedent irradiation therapy. On the basis of biopsy or necropsy material from the primary growth or from metastatic lesions,

the tumor was classified as lymphoma or lymphoepithelioma in five cases, as epidermoid carcinoma in four, and as undifferentiated carcinoma in two.

Although we have been concerned chiefly with the cranial nerve palsies resulting from extension of malignancy in the nasopharynx, it is not implied that the production of such syndromes by neoplastic invasion is limited to tumors originating from this site. Progressive cranial nerve involvement was recently observed in an 18-year-old girl in whom malignant lymphoma of the thoracic and abdominal cavities was demonstrated at necropsy. In this case no neoplastic tissue was found in the skull or nasopharynx, but dissemination of malignant cells had occurred throughout the subarachnoid space. Similar findings were reported by Sparling, Adams, and Parker [6] in a case of lymphatic leukemia complicated by cranial nerve palsies.

Cranial nerve damage due to primary involvement of the base of the skull in a patient with multiple myeloma has been observed by Clarke,[7] who, in addition, collected 24 similar cases from the literature.

Summary

Eleven cases in which cranial nerve palsies were an early or conspicuous manifestation of malignancy of the nasopharynx are presented. Necropsy studies on eight of these cases suggest that involvement of the cranial nerves may result from subdural extension of the growth or from neoplastic infiltration of the subarachnoid space, as well as from implication at the foramina of the skull. Cranial nerve lesions may also follow neoplastic invasion from sites other than the nasopharynx.

133 South 36th St. (4) (Dr. Rupp).

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Cerebrovascular Accidents in Patients with Congenital Heart Disease

H. RICHARD TYLER, M.D., and DAVID B. CLARK, M.D., Baltimore

Introduction

Cerebrovascular accidents have long been recognized as a complication of congenital heart disease and are mentioned by Batten,[1] White,[2] Abbott,[3] Ford,[4] and others. Berthrong and Sabiston[5] reported on cerebral lesions in 162 cases of congenital heart disease. Taussig[6] emphasized their occurrence in congenital heart disease and related them to polycythemia and low oxygen content of the blood.

In an earlier paper[7] we presented the incidence of various neurologic complications not related to cardiac surgery in 1875 patients with congenital heart disease. Seventy-two patients in our series had suffered a cerebrovascular accident. The present report is based on an analysis of their records. All of these patients have been seen and followed by the cardiac clinic of the Harriet Lane Home, The Johns Hopkins Hospital.

Received for publication June 12, 1956.

Subdepartment of Neurology, Department of Pediatrics, The Johns Hopkins Hospital. Fellow of the National Foundation for Infantile Paralysis (Dr. Tyler).

I. Incidence in Congenital Heart Disease

The incidence of cerebrovascular accidents varied with the type of congenital malformation of the heart. In general, the highest incidence of cerebrovascular accidents occurred in those patients with forms of congenital heart disease that produced the severest cyanosis and hypoxia in the first two years of life, i. e., transposition, tricuspid atresia, etc. The distribution of these cases is given in the accompanying Table, which also appeared in our initial paper.[7]

II. Clinical Data

The vast majority of hemiplegias occurred in the first 20 months of life, i. e., 53 out of 72, or 73.6%. They were seen with decreasing frequency through the sixth year and then were not seen again until the middle teens (Fig. 1). Of those occurring in the first six years, 57 out of 64, or 89.1%, persisted, whereas only 4 out of 8 of those occurring after 16 years of age persisted; the others were transient, and the patients showed no neurologic residua.

Incidence of Cerebrovascular Accidents with Congenital Heart Disease

Form of Congenital Heart Disease	No. of Cases with Cerebrovascular Accidents	Total No. of Cases	Percentages (When Significant)
Tetralogy of Fallot	41	1,045	3.9
Tricuspid atresia and stenosis	2	18	--
Single ventricle	0	10	--
Transposition with pulmonary stenosis	2	16	--
Single ventricle with pulmonary stenosis	1	10	--
Truncus arteriosus with decreased flow	1	94	1.1
Transposition	12	109	11.0
Transposition with tricuspid atresia	0	4	--
Ebstein's malformation	3	19	--
Pure pulmonary stenosis	6	110	5.5
Truncus arteriosus with normal flow	0	10	--
Eisenmenger's syndrome	3	123	2.4
Truncus arteriosus with increased flow	0	10	--
Interventricular and interauricular septal defects	0	138	0.0
Patent ductus arteriosus	1	159	0.6
Total	72	1,875	3.8

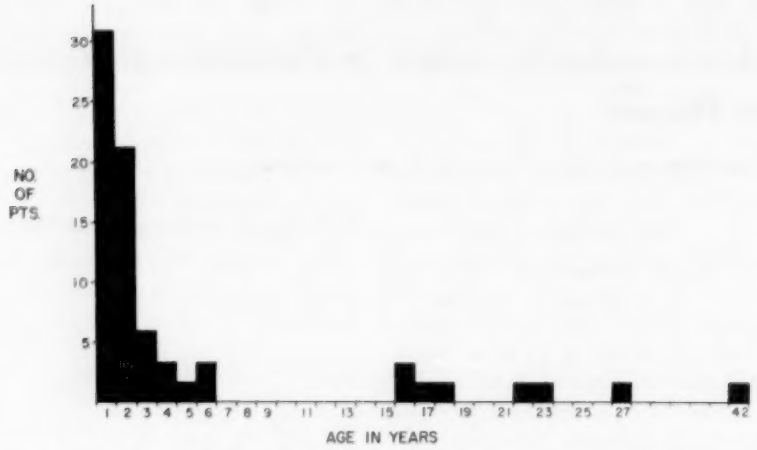

Fig. 1.—Graph showing age distribution of patients with cerebrovascular accidents. Age is given at the time of the neurologic complication.

Thirty-four hemiplegias were on the left side and 33 on the right side. Four patients had a bilateral hemiplegia, and one patient had clinical signs of an infarction of the brain stem.

In 25 patients the history of onset was detailed enough to permit analysis.

Fifteen patients were suffering from some acute illness, in which fever and dehydration may have been of significance. Five patients had a convulsion, or series of convulsions, which ended in a permanent hemiplegia. Three patients had their hemiplegia develop after an acute cyanotic and dyspneic attack of unusual severity. Two patients were "cutting teeth," the description given when they had an unexplained fussy and fretful period from two to three days prior to the hemiplegia. In only one case were dehydration and hot weather clear precursors. It is apparent from Figure 2 that there is no real seasonal incidence.

III. Role of Oxygen and Polycythemia

Figure 3 gives the oxygen content of the arterial blood in 15 patients at the time of their hemiplegias. In all cases where patients were under 2 years of age oxygen content was below 10%. The five older patients had their hemiplegias at a time when oxygen content was nearly normal, or normal.

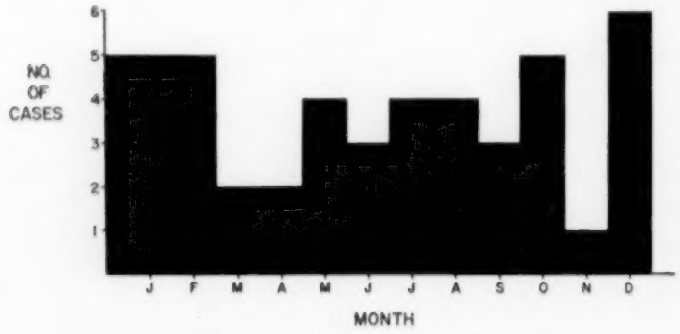

Fig. 2.—Graph showing month that cerebrovascular accident occurred.

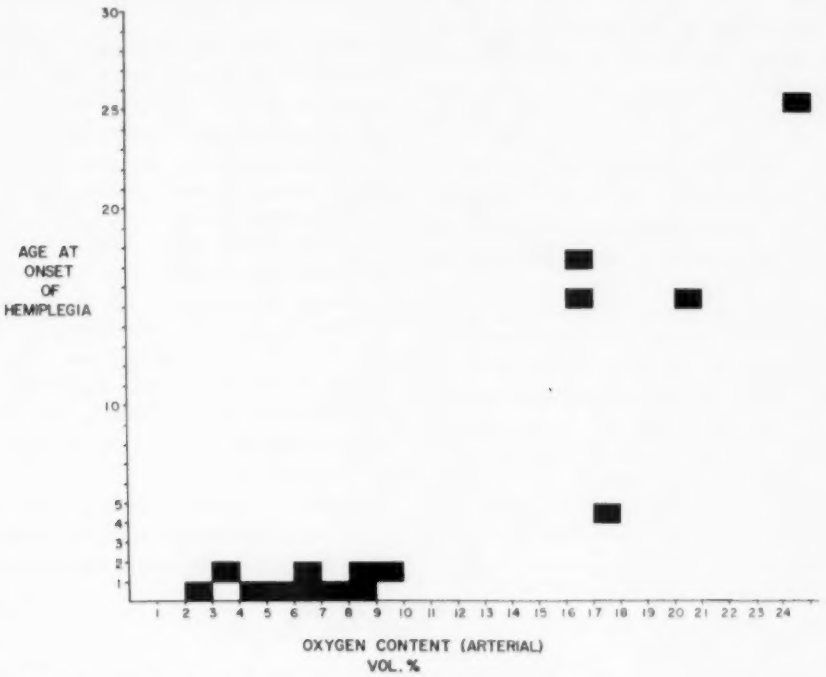

Fig. 3.—Graph demonstrating 15 patients (black squares) who had arterial oxygen content determinations done at the time of their cerebrovascular accident. This graph should be compared with Figures 4 and 5.

In Figure 4 is plotted the relationship of oxygen saturation to age. Again, it is noted that in the older patients the oxygen saturation was relatively high, while in those under 2 years it was below 53%. This suggests that hypoxia was not important as an etiological factor in the older age groups.

Figure 5 shows the magnitude of the red blood cell count at the time of hemiplegia in 17 patients. In all of the older patients the red blood cell count was above 8,000,000. In 11 of the 12 patients under 2 years of age the red blood cell count was below 8,000,000.

In the younger group polycythemia did not appear to be as important a factor as in the older patients. Some young patients developed hemiplegia at a time when they were not polycythemic.

IV. Sequelae

Forty-two patients were followed long enough to evaluate their mental progress. Eight, or 19%, had mental retardation of some severity. All of these had suffered their hemiplegias in the first two years of life.

In our original series, of 1875 patients with congenital heart disease,[7] 107 had some degree of mental retardation. These hemiplegic patients, therefore, represented 7.5% of the total number of defectives found in the original survey.

Seven out of sixty, or 11.5%, had a convulsive disorder which followed the hemiplegia and seemed to be directly related to it. It began, characteristically, after a latent period of from six months to five years after the hemiplegia and tended to be severe and difficult to control.

V. Pathology

Fourteen patients came to autopsy. Only one died primarily as a result of his hemiplegia. An unsuccessful attempt at cardiac

surgery was the cause of death in most of the other patients. All showed large infarctions in the distribution of the middle cerebral artery. In only three of these cases was it possible to prove directly that the middle cerebral artery was abnormal, however, a definite thrombosis being found.

Two of the patients had large porencephalic cysts secondary to infarction, and in another patient a large porencephalic cyst was seen at operation.

In only one patient was venous thrombosis noted. This patient had a hemiplegia at 6 months and lived to 14 months of age, dying after a severe acute illness with dehydration. There was an old infarction in the right hemisphere in the distribution of the middle cerebral artery, and a recent transverse sinus and inferior sagittal sinus thrombosis with new infarctions in the left hemisphere.

VI. Differential Diagnosis

It was obvious that there were many other conditions which had to be differentiated. Cerebral abscess was perhaps the commonest and the most important to distinguish from cerebrovascular accidents. The hemiplegia associated with abscess was usually more gradual in onset, though rarely sudden. In patients with cerebral abscess headaches, abnormal spinal fluids, and more diffusely abnormal EEG's were all useful in differentiating the two conditions. It should also be noted that cerebral abscess in congenital heart disease has only once been reported in a child under 2 years, whereas the majority of vascular hemiplegias have occurred by then.

Cerebral tumor was seen in two of the children. The gradual onset of symptoms, i. e., headaches and other signs, served to

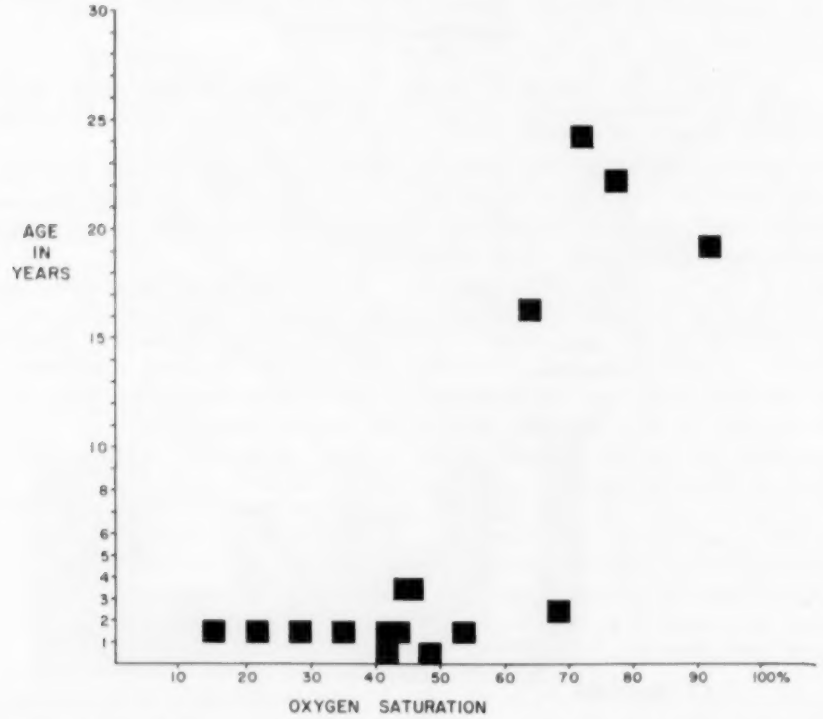

Fig. 4.—Graph demonstrating 16 patients (black squares) who had oxygen saturation determinations done at the time of their hemiplegia.

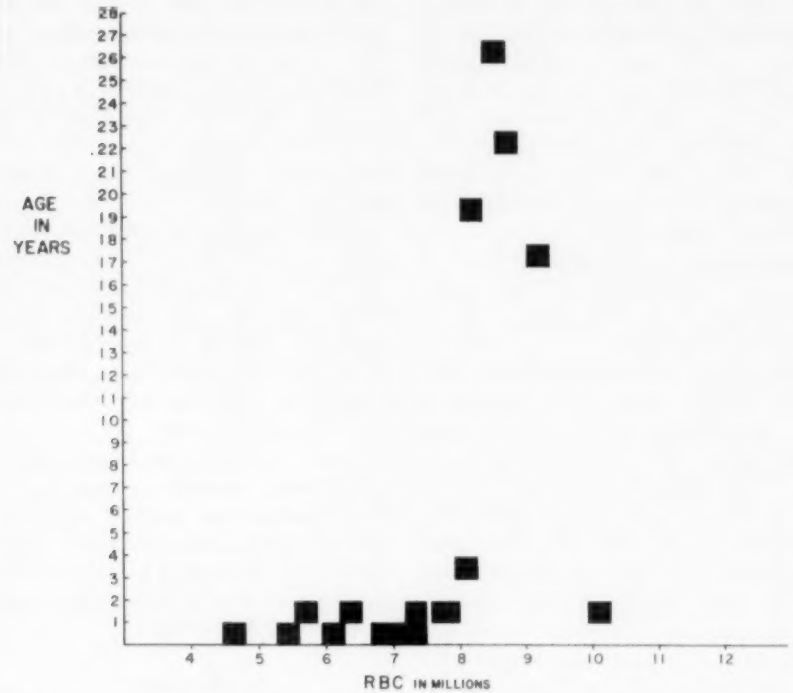

Fig. 5.—Graph demonstrating 17 patients (black squares) who had a red blood cell count done at the time of their cerebrovascular accident.

differentiate these cases. Two patients with hemiplegia following trauma have also been observed. One of the patients had a subdural hematoma; the other, a chronic epidural hematoma, which did not present for 41 days. One child had a birth injury with hemiplegia dating from birth. This diagnosis was obvious from the history alone.

Comment

With the steady growth of cardiac surgery, the clinician can now offer many patients with congenital heart disease the hope of alleviation and improvement of the cardiac status.

Fear of cerebral complications is often a major motivating cause in advising cardiac surgery. Our knowledge of the etiology of these complications stems from the experience of White,[2] Taussig,[6] and others. White[2] states:

> . . . equal in importance to respiratory and pulmonary symptoms are those of cerebral nature chiefly due to anoxia, but in cases of considerable polycythemia they are due to sluggish circulation and to cerebral thrombosis.

Taussig[6] writes:

> Cerebral thrombosis is a common complication. It is often the result of the increased viscosity of the blood but may occur in an infant with severe anoxemia without polycythemia. Dehydration greatly increases the danger of thrombosis.

The vast majority of cerebrovascular accidents occur in the first two years of life. They are seen predominantly in those forms of congenital heart disease in which the symptoms are severest during that period. This appears to be the best explanation for the varying incidence of cerebrovascular accidents in the various forms of congenital heart disease.

No definite seasonal incidence was found. The commonest correlation noted was the occurrence, in the majority of patients, of an acute illness at the time of the hemiplegia. Fever and dehydration, as such, were probably two important factors in this connection. The added strain and increased nutritional demands of an ill child may well have been a factor also.

In the younger age group (2 years or under) both oxygen content and polycythemia seemed to play important roles in the production of cerebrovascular accidents. There was often an inverse relation between the two. If the hypoxia was sufficiently severe, then the cerebrovascular accidents occurred at normal red blood cell count levels. As the red blood cell count rose, the degree of hypoxia needed was progressively less. If the red blood cell count was higher than 8,000,000, no significant hypoxia was needed to cause a cerebrovascular accident.

The critical level of hypoxia in our patients appeared to be an arterial oxygen content of 10 (50% normal). If the level of oxygen was above this level, only patients with a high degree of polycythemia (8,000,000 or over) suffered cerebrovascular accidents.

Schmidt's[8] observation that cerebral respiratory metabolism in normal man does not vary until oxygen content is decreased below 10% provides an experimental confirmation of the clinical observations made in these cases. The importance of this critical level of hypoxia, i. e., an arterial oxygen content of 10, cannot be underestimated and is probably as important as the factor of polycythemia.

The older patients (those above 16 years of age) all had a red blood cell count above 8,000,000 and had no significant hypoxia. In these patients polycythemia alone appeared to be the major factor.

We were not able to establish an embolic origin in any patient in this series. It is our belief that the vast majority of these patients suffered from cerebral thrombosis. The postmortem material, age distribution, relationship to precipitating factors, correlation to polycythemia, and hypoxia all are in favor of this presumption. Two patients, not included in the original series because of previous cardiac surgery, had transient hemiplegias during the course of subacute bacterial endocarditis. One was 7 years of age and the other 9. In both cases the oxygen content was high and the polycythemia was minimal (5,400,000 and 5,860,000). The age and absence of either significant hypoxia or polycythemia, combined with the sudden onset, suggested the diagnosis of embolism, rather than thrombosis, in these two cases.

In 14 of our cases the lesions noted postmortem were arterial in distribution. None of the postmortem material was from the older age group, however, and it is possible that venous infarctions or emboli accounted for some of the cerebrovascular accidents in the remaining patients.

Summary

Cerebrovascular accidents are common complications of congenital heart disease. In a series of 1875 patients, 72, or 3.8%, have this complication. The majority of cerebrovascular accidents in this series occur during the first two years of life. They are most frequently seen in those forms of cyanotic heart disease which produce the severest hypoxia and polycythemia in the first two years of life, i. e., transposition.

There is no seasonal incidence.

In younger patients hypoxia seems to play a role as important as polycythemia. In older patients polycythemia seems to be the major precipitating etiological factor.

All of our patients who have suffered a cerebrovascular accident have a red blood cell count above 8,000,000 or an arterial oxygen content below 10 volumes per cent.

Nineteen per cent of the survivors are mentally retarded.

Eleven per cent have convulsive disorders following their hemiplegias.

In all 14 patients coming to autopsy infarction is shown in the distribution of the middle cerebral artery.

Dr. Helen B. Taussig allowed us access to the patients and records of her clinic.

The Johns Hopkins Hospital (5).

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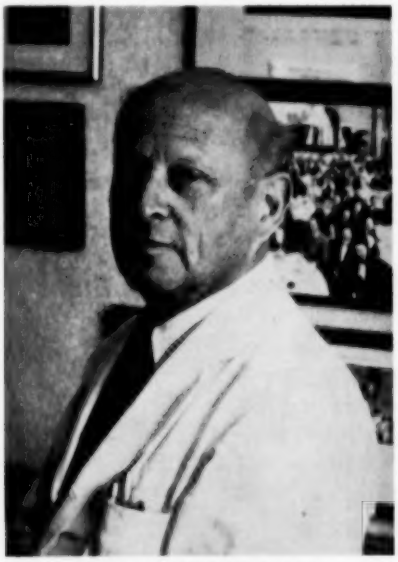
Obituaries

ROBERT WARTENBERG, M.D.

1887-1956

The death of Robert Wartenberg, on Nov. 16, 1956, has taken a colorful figure from clinical neurology. Wartenberg had two brilliant careers, an initial one in Europe and a later one in America. He delighted in the descriptive phase of clinical neurology, and especially in the elaboration of new reflexes and signs. Of the four books he wrote, "Examination of Reflexes" and "Diagnostic Tests in Neurology," as well as the bulk of his 156 scientific papers, clearly reflect this major interest, as did the thoroughness evident in all his writings. As an editor and critic he was meticulous and painstaking. He was a member of the editorial boards of *Confina neurologica, Neurology,* and *The Journal of Nervous and Mental Disease* and gave editorial assistance to many others.

Wartenberg loved to teach. The dramatic quality of his clinical demonstrations, the mastery of his subject, his infectious enthusiasm, and his emphasis on fundamentals made each lecture an occasion. For years he gave a widely popular elective course at the University of California School of Medicine (San Francisco). Inevitably he was mimicked by the students in their annual play, which Wartenberg always enjoyed. He was annually voted their best teacher.



ROBERT WARTENBERG, M.D.

1887-1956

Born in Grodno, on the German border of Russia, June 19, 1887, he studied medicine at the Universities of Kiel, Munich, Freiburg, and Rostock, receiving his medical degree *magna cum laude* from the last university in 1919. He worked

under such eminent men as Professors Hoche, of Freiburg; Cassirer, of Berlin; Nonne, of Hamburg, and Foerster, of Breslau. In 1925, as a fellow of the Rockefeller Foundation, he visited teaching centers of neurology in England, France, and the United States. On his return to Freiburg, he was made physician-in-chief of the neurology clinic in 1930 and became *ausserordentlicher Professor* of neurology and psychiatry.

In 1935, with the rise of Hitler, Wartenberg left Germany and started his second career at the University of California School of Medicine in 1936. He was made clinical professor of neurology in 1952. After retirement, in 1954, he continued his editorial work and writing. Just two hours before his final illness, he completed a book, "Neuritis, Sensory Neuritis, Neuralgia."

A *Festschrift* entitled "Neurological Problems in the World in 1953," honoring Wartenberg on the occasion of his sixty-fifth birthday, was published as the December issue of *The Journal of Nervous and Mental Disease* for 1952. Dr. Wartenberg was an honorary member of various neurological societies of Spain, Italy, Germany, Austria, Brazil, and Argentina.

In 1954 the University of Freiburg invited him as guest professor of neurology and the following year made him honorary professor.

In spite of his many honors, Wartenberg was a man of simple taste. His main joy was his home life, with his beloved wife, Isabelle, and his father-in-law, Baron Karl von Sazenhofen, who survive him. Their personal loss is shared by his friends in the University of California and that wider circle of friends throughout the world in the field of clinical neurology.

ROBERT B. AIRD, M.D.

Abstracts from Current Literature

Surgical Treatment of Arteriovenous Malformations of the Brain. R. A. Hayne, L. G. Kempe, and W. Coxe, J. Neurosurg. 13:259 (May) 1956.

The authors report nine cases of arteriovenous malformations of the brain which were treated surgically, by total excision in six cases and by ligation of a single afferent artery in two others. In the remaining case an arteriovenous malformation in the region of the third ventricle produced an obstructive type of hydrocephalus, which was corrected by means of a ventriculocisternostomy shunt. The authors believe that preliminary ligation of the external carotid arteries should be performed when these vessels contribute to the blood supply of the arteriovenous malformation.

Since the clinical course of these malformations is characterized by subarachnoid hemorrhage and intracerebral hematoma with secondary hemiparesis, early carotid arteriography is stressed, for such patients require early surgical treatment. In each of the nine cases which were treated surgically the patient was able to resume essentially the same type of activity as that engaged in prior to the onset of symptoms.

Mandel, Philadelphia.

Fate of Patients Who Have Cerebral Arteriovenous Anomalies Without Definitive Surgical Treatments. H. J. Svien, I. Olive, and P. Anguilo-Rivero, J. Neurosurg. 13:293 (July) 1956.

Cerebral arteriovenous anomalies frequently occur in the Rolandic and Sylvian fissures and are accompanied by an operative mortality rate of 11.7%. Because of this risk involved, many patients receive no definitive treatment.

The authors report their findings in 51 patients having cerebral arteriovenous anomalies which were verified either by surgical exploration or by cerebral arteriography. Of this group, 23 received no definitive treatment, and the results are reported from the standpoint of the usual symptoms encountered in these cases.

In the series of 23 patients, 9 (39.1%) had intracranial bleeding. Seven of these patients had subarachnoid hemorrhages, and two had a history and physical findings typical of intracerebral hematoma. Of the seven patients who had subarachnoid hemorrhage, two died during their first episode, one had Jacksonian seizures for 22 years, and the other had temporal lobe attacks for 2 years. The mortality rate from intracranial bleeding was 8.7% in this group. The authors concluded that, because of the high mortality rate of radical extirpation of these lesions and the fact that excision cannot always be complete because of the inaccessible location of the lesions, intracranial bleeding is not an indication for surgery.

Convulsive disorders were found in 15 of 23 patients; 6 patients had generalized seizures; 6 had Jacksonian seizures, and 3 had temporal lobe attacks. The majority of these cases were controlled by medication, and surgery would not have been considered. In two cases, with temporal lobe attacks, the inaccessible location precluded surgical intervention, again because of the high surgical mortality rate.

Progressive hemiparesis developed in 13% of patients in this series. This figure corresponded to the mortality rate of surgical extirpation, and in most cases the neurologic defect produced by surgery was as pronounced as those without surgical treatment.

Mental deterioration was found in only one case, and headaches did not constitute an indication for surgical intervention.

Mandel, Philadelphia.

Experiences with Corticotropin and Cortisone in Organic Diseases of the Nervous System. S. Feldman and D. P. Kidron, Monatsschr. Psychiat. u. Neurol. 132:96 (Aug.-Sept.) 1956.

Feldman and Kidron describe experiences in the use of corticotropin and cortisone in various neurological disorders. Twenty-four patients with multiple sclerosis, mostly of several years' duration, were given this treatment. Of six patients with acute

exacerbations, five appeared to have benefited significantly in terms of some rather prompt improvement or recovery of the recently affected function. Eighteen "chronic" cases were virtually unaltered. It should be noted that those patients whose acute phases subsided with the administration of hormone treatment were patients who had experienced recent acute relapses with remission, and the follow-up periods of less than one year are insufficient to permit conclusions concerning the influence of this treatment on the course of the illness. However, two additional cases, one of the Guillain-Barré syndrome and the other of postmeasles encephalitis, appeared to have been markedly influenced by the administration of corticotropin treatment; both these responsed positively and favorably within a 24-28-hour period, with relapses closely following withdrawal of the medicament. Corticotropin reversal of lesions in experimental homologous injection encephalomyelitides, as well as the favorable trend frequently noted succeeding therapy in such conditions as vaccinial (antivaricellar and antirabic) and other forms of disseminated encephalomyelitis suggests that antihyperergic effects may constitute the basis of therapeutic action.

PARSONS, Montrose, N. Y.

Muscular System

MUSCULAR DYSTROPHY: I. HISTORY, CLINICAL STATUS, MUSCLE STRENGTH, AND BIOPSY FINDINGS. G. H. FETTERMAN, M. J. WRATNEY, J. S. DONALDSON, and T. S. DANOWSKI, A. M. A. J. Dis. Child. 91:326 (April) 1956.

The authors studied 31 cases of the juvenile form of muscular dystrophy and concluded (1) that the developmental history often indicated retardation in walking; (2) that all muscle groups were involved, usually symmetrically so, and the lower limbs more than the upper limbs; (3) that the microscopic preparations showed (intermingled with normal fibers) swollen, degenerated, or atrophic individual muscle fibers, some split and eroded and some undergoing phagocytosis, and very rarely rows of sarcolemmal nuclei within the central portions of the fiber; (4) that the histologic lesions are always far advanced in patients with pronounced muscle weakness and that histologic changes may precede clinical evidence of muscle weakness; (5) that removal of biopsy tissue does not cause further deterioration in muscle strength, and (6) that the spinal fluid is normal.

SIEKERT, Rochester, Minn.

MUSCULAR DYSTROPHY: II. RADIOLOGIC FINDINGS IN RELATION TO SEVERITY OF DISEASE. B. GIRDANY and T. S. DANOWSKI, A. M. A. J. Dis. Child. 91:339 (April) 1956.

In roentgenographic surveys of patients with muscular dystrophy the authors observed that (1) degree and frequency of scoliosis (2) apparent increase in altitude of vertebral bodies; (3) valgus deformity of the proximal femur; (4) subluxation of the hip; (5) changes in the long bones (except the forearm ones), consisting of narrowing of the shaft and overtubulation of the metaphysis; (6) striation of soft tissues from infiltration of fat, and (7) osteoporosis are all directly related to the extent of the disease process. Lordosis is not related to extent of the disease.

SIEKERT, Rochester, Minn.

MUSCULAR DYSTROPHY: III. SERUM AND BLOOD SOLUTES AND OTHER LABORATORY INDICES. T. S. DANOWSKI, P. M. WIRTH, M. H. LEINBERGER, W. A. RANDALL, and J. H. PETERS, A. M. A. J. Dis. Child. 91:346 (April) 1956.

In the infantile form of muscular dystrophy the fasting level of creatine in the serum is higher than in normal persons. In 45 minutes after oral administration of creatine there is no difference between normal and dystrophic subjects in the degree of serum elevation of creatine, but after 135 minutes the elevation is still present in patients with dystrophy. This intolerance to creatine in dystrophic people is attributed to reduced muscle uptake (reduced mass of muscle).

Serum phosphorus and calcium values are increased in dystrophy; cholesterol and chloride values are lower. Although no explanation is known, the high calcium may reflect immobilization and osteoporosis, while the high phosphorus may be related to the creatine intolerance.

Other serum and blood solutes, formed elements, hematologic intices, and tests for kidney and liver function are normal.

SIEKERT, Rochester, Minn.

MUSCULAR DYSTROPHY: IV. ENDOCRINE STUDIES. T. S. DANOWSKI, R. M. BASTIANI, F. O. MCWILLIAMS, F. M. MATEER, and L. GREENMAN, A. M. A. J. Dis. Child. 91:356 (April) 1956.

The amount of corticoids in the serum, the urinary excretion of pituitary gonadotropin and 17-ketosteroid, and the response of the eosinophils to corticotropin are normal in children with muscular dystrophy.

The protein-bound iodine of the serum tends to be higher in patients with muscular dystrophy, while the cholesterol in the serum tends to be lower than normal. Glucose tolerance tests give normal results; insulin tolerance tests show less hypoglycemia (capillary blood sugar) in dystrophic subjects, representing a decreased acceleration of glucose metabolism.

SIEKERT, Rochester, Minn.

MUSCULAR DYSTROPHY: V. BLOOD SUGAR AND SERUM ELECTROLYTES FOLLOWING INSULIN AND DEXTROSE, ALONE OR IN COMBINATION. T. S. DANOWSKI, H. K. GILLESPIE, T. J. EGAN, F. M. MATEER, and M. H. LEINBERGER, A. M. A. J. Dis. Child. 91:429 (May) 1956.

The authors conclude that in muscular dystrophy the inadequate disposal of glucose from exogenous (and perhaps endogenous) sources is due to decreased extrahepatic (i. e., muscular) utilization.

SIEKERT, Rochester, Minn.

MUSCULAR DYSTROPHY: VI. DIMINISHED BLOOD SUGAR AND SERUM ELECTROLYTE RESPONSES TO EPINEPHRINE. E. B. FERGUS, W. R. NICHOLS, L. M. HORNE, and T. S. DANOWSKI, A. M. A. J. Dis. Child. 91:436 (May) 1956.

The subcutaneous administration of epinephrine produces a smaller degree of hyperglycemia in patients with muscular dystrophy than in control subjects. While the cause of this is unknown, the data are compatible with functionally defective or decreased stores of muscle glycogen.

SIEKERT, Rochester, Minn.

MUSCULAR DYSTROPHY: VII. TRIALS OF A PITUITARY GROWTH FACTOR. T. S. DANOWSKI, L. GREENMAN, F. M. MATEER, M. T. WRATNEY, and J. S. DONALDSON, A. M. A. J. Dis. Child. 91:442 (May) 1956.

A preparation of pituitary growth factor, active in producing growth in hypophysectomized mice, was clinically ineffective in children with muscular dystrophy.

SIEKERT, Rochester, Minn.

MUSCULAR DYSTROPHY: VIII. TRIALS OF PROTEIN HYDROLYSATE, VITAMIN SUPPLEMENTS, AND PHYSICAL THERAPY. T. S. DONALDSON, M. J. WRATNEY, A. PASCASSIO, F. A. WEIGAND, and T. S. DANOWSKI, A. M. A. J. Dis. Child. 91:449 (May) 1956.

The administration of protein hydrolysate and vitamins was without clinical benefit to patients with muscular dystrophy.

SIEKERT, Rochester, Minn.

MYASTHENIA GRAVIS: A PERSONAL STUDY OF 60 CASES. HUGH GARLAND and A. N. G. CLARK, Brit. M. J. 1:1259 (June 2) 1956.

Garland and Clark reviewed the records of 60 patients with myasthenia gravis observed by one of them in 15 years of civilian private and hospital practice and traced from 1934 to September, 1955. In 65% of cases the age of onset of symptoms was between 21 and 50 years, with a range of 6 to 75 years. The shortest duration of symptoms was 1 year and the longest 28 years. Twelve patients had only ocular manifestations, and only five at no time complained of ocular symptoms. Although the disease is characterized by daily fluctuations and partial or complete remissions, 50% of the present series had never had a complete remission.

The prognosis of the disease has been greatly improved with the discovery of neostigmine (Prostigmin). The authors believe that each patient should be given as

much of the drug as he needs to control his disability. Four of their patients "have taken 1000 mg. a day, or more, sometimes for long periods and one has had an average daily dose of 600 mg. for nearly 20 years." Their experience with other methods of treatment, including thymic irradiation, thymectomy, and pyridostigmine, and tetraethylpyrophosphate, is too small to be significant. Of 53 patients who could be traced, 9 have died of the disease.

ECHOLS, New Orleans.

MYOPATHIES AND FUNCTIONAL DISTURBANCES IN MUSCLES. N. ZEC, Monatsschr. Psychiat. u. Neurol. 130:161 (Aug.) 1955.

Zec proposes a unitary concept of neuromuscular disturbances based on a theory of a bineuronal somatic motor impulse transmission system analogous to the autonomic plan, wherein the anterior cornual cell represents the first element and the motor end-plate (regarded by this author as a phylogenetically derived peripheral ganglion cell) is believed to constitute the second element of the system. Neuromuscular disorders are divided into two groups: one in which the first (neuraxial) neuron is primarily affected, giving rise to impairment of the selective central inhibition and encompassing such diseases involving an increase in tone or activity as the various myotonias, as well as fasciculations. The second group is considered to represent dysfunction at the end-plate (or second neuron) level and includes disorders characterized by decrease of muscular tone or activity, such as amyotonias, myasthenia, and periodic paralysis. The author supports these statements with a discussion of certain biochemical studies (i. e., potassium, creatine-creatinine, etc.), wherein have been noted contrasting fluctuations in various examples of the two groups of disorders, and also by citing examples of mixed syndromes, one of which, involving a combination of muscular dystrophy and periodic paralysis, is presented in detail.

PARSONS, Montrose, N. Y.

Encephalography, Ventriculography and Roentgenography

ROENTGENOGRAPHIC SIGNS OF TUMORS OF THE BRAIN. E. L. GILBERTSON and C. A. GOOD, Am. J. Roentgenol. 76:226 (Aug.) 1956.

Gilbertson and Good reviewed all cases of proved intracranial neoplasms seen at the Mayo Clinic between January, 1940, and January, 1945. In order that a case be included in the series presented in this paper, the site of the tumor had to have been determined either at operation or at autopsy, there had to be histologic proof of the nature of the tumor, and a good set of roentgenograms of the skull had to be available for study. A total of 661 cases met these criteria. The study did not include special roentgenographic procedures or studies using contrast media. On plain roentgenograms of the skull there are two general types of signs: localizing signs and general signs of increased intracranial pressure. There are six roentgenologic signs which help both to diagnose and to locate brain tumors: (1) calcification within the lesion, (2) pineal and/or choroid shift, (3) hyperostosis and osteomatous formation, (4) erosion or destruction of bone, (5) erosion of sella turcica (in intrasellar tumor), and (6) increased vascularity. There are five general signs of increased intracranial pressure: (1) erosion of sella turcica, (2) separation of sutures, (3) hydrocephalus, (4) convolutional atrophy, and (5) increased vascularity. Of the 661 cases in this series, 64% showed positive signs of an intracranial lesion on the plain roentgenograms of the skull. The highest degree of positive findings was within the group of pituitary adenomas, where 95% of the cases showed positive findings. In 71% of meningiomas and 53% of gliomas findings were positive.

Of the 326 gliomas found, 136 were glioblastomas. Calcification occurred in less than 5% of the glioblastomas, and pineal displacement also was infrequent. Medulloblastomas showed no calcification or pineal shift. Thirty-five oligodendrogliomas were found, and a little more than half of them showed calcification. Thirteen per cent of the 98 astrocytomas showed calcification. Gliomas rarely produced localized bone change except for erosion of the sella turcica, which occurred sometimes from direct pressure and sometimes because of pressure from the obstructed ventricular system.

Calcification occurred in 18% of the meningiomas, and some type of bone reaction in the skull was seen in about 45%. Thirty-six per cent of the cases of meningiomas

showed erosion of the sella turcica. Twenty-nine chromophobe adenomas of the pituitary were found. These tumors practically all produced some degree of erosion of the sella turcica. Intrasellar tumors expanded the sella turcica in a uniform circular manner, which was easily recognized in the early stages. Finally, however, there was complete destruction of the dorsum sellae, and then it was difficult for the examiner to determine whether the tumor was likely to be extrasellar or intrasellar in origin. Seventy-six per cent of 25 cases of craniopharyngioma showed positive findings. Calcification was present in 68% of these cases, and erosion of the sella turcica was present in the other positive ones.

The findings in carcinomas, sarcomas, hemangiomas, angiomas, hemangioblastomas, epidermoids, and other rare tumors are also listed.

WEILAND, Grove City, Pa.

MYELOGRAPHY OF COMPLETE SPINAL OBSTRUCTION. A. S. TUCKER, Am. J. Roentgenol. 76: 248 (Aug.) 1956.

Of 196 consecutive myelographic examinations performed between 1949 and 1953, Tucker found obstruction of the spinal canal in 75. The presence of complete obstruction in about 39% of all the myelograms obtained is explained by the fact that Tucker and his associates consider myelography a hazardous procedure and limit its use to those cases in which they feel the information that they are likely to obtain will be particularly helpful in the management of the case. During the same period of observation 689 laminectomies were performed. Only about 28% of these were preceded by myelographic study. Myelography is not used frequently in patients suspected of having herniated intervertebral discs.

All but 1 of the 75 cases with the diagnosis of a complete block in the spinal canal were verified surgically; in the other case operation was not done. In addition, there were two patients during the same period of time for whom the diagnosis of a complete block was made because of myelographic findings who were found not to have a block when explored surgically. Over half the blocks were encountered in the thoracic region of the spine. It is possible to determine something concerning the nature of the blocking agent by studying the configuration of the opaque medium as it reaches the blocked area. If the contrast medium moves slowly and breaks up into globules, subarachnoid adhesions are likely. If the contrast material stops abruptly and the end of the opaque column assumes a concave form, it is likely that there is some intradural form of obstruction. If the column ends abruptly but frays out or is funneled into a narrowed channel, there is a strong probability that the lesion is of extradural origin.

Very few intramedullary lesions produced the block in this series of cases. Neurofibromas, meningiomas, malignant tumors, and herniated intervertebral disks accounted for 70% of the obstructions. Most of the neurofibromas were extradural in origin. All the malignant tumors were extradural (carcinoma, lymphoma, sarcoma, and myeloma). A few benign tumors also were found to produce complete blocks. One teratoma, one hemangioma, and one hemangiopericytoma were found.

WEILAND, Grove City, Pa.

MEASUREMENT OF THE CERVICAL SPINAL CORD IN PANTOPAQUE MYELOGRAPHY. E. C. PORTER, Am. J. Roentgenol. 76:270 (Aug.) 1956.

The width of the cervical portion of the spinal cord has previously been estimated by obtaining films taken at 6 ft., in the lateral projection, of people undergoing pneumoencephalography. The air in the subarachnoid space makes the subarachnoid space visible and its width measurable. Porter measured the width of the opaque column in films which he took during cervical myelography on 65 patients. Since the films used were "spot" films, there was no fixed or consistent target-film distance or part-film distance. The distances varied from one film to the next. There is considerable and variable magnification of the image under these conditions. The levels of the fourth and sixth cervical vertebrae were arbitrarily chosen for measurement, but circumstances often made it impossible to measure at both levels, so that either one which happened to show up well was measured. Of these 65 patients, 63 showed either herniated intervertebral disks or no abnormality at the surgical operation which followed the myelography. The width of the column of iophendylate (Pantopaque) in the cervical subarachnoid spaces of these patients ranged from a minimum of 1 cm. to a maximum of 1.7 cm.

The other two patients had intramedullary tumors of the cord. The maximum width of the opaque column was 2.7 cm. in one and 2.2 cm. in the other. Porter concluded from the 63 normal cases and the 2 abnormal cases that a measurement of 1.8 cm. or higher should be regarded with suspicion and that a measurement of 2.0 cm. or over is abnormal, provided that the same method of obtaining and measuring the films is used.

WEILAND, Grove City, Pa.

IMPORTANCE OF MYELOGRAPHY IN SPINAL PATHOLOGY. F. J. BORRELLI and A. A. MAGLIONE, Am. J. Roentgenol. 76:273 (Aug.) 1956.

Borrelli and Maglione reviewed 150 cases in which myelography was performed during the period of 1950 to 1953. Their routine in this procedure is to take plain films of the lumbar spine before performing the myelography. When these films have been made and interpreted, the myelogram is obtained by injecting iophendylate (Pantopaque) into the spinal canal at the level of the third lumbar interspace. Injection of 3 cc. of the opaque medium is done for lumbar myelography and of 6 cc. for cervical myelography. Borrelli and Maglione feel that the lumbar myelograms they have taken using more than 3 cc. of the opaque medium have given no more information than the ones obtained using the smaller amount. The routine exposures are used anteroposterior and lateral, both views being taken with the patient lying prone. It is necessary to use a horizontal ray to take the lateral view with the patient lying prone.

Spinal umors may give rise to different myelographic filling defects. The following types are encountered: (1) Fusiform filling defect with absence of clear-cut margins. This type of defect is characteristic of intramedullary tumors of the cord. 2. Sharply defined rounded defect and concave defect. These defects are characteristic of intradural tumors. 3. Pressure indentation defect. This defect is usually seen in extradural tumors. 4. Incomplete or complete block of the opaque column. This may be produced by any spinal cord tumor or by a large herniated intervertebral disk.

Deformities found with herniated intervertebral disks also are described. The unilateral filling defect is the most frequent type of deformity. A bilateral hourglass deformity is sometimes found. A large herniation can cause a block or complete obstruction in the spinal canal. An anterior indentation in the opaque column demonstrated in the prone lateral view (transvertebral view) is found in some cases of herniated disk when no other evidence of herniation can be demonstrated. The "veil" defect consists of visualization of an area of decreased density within the opaque column but is a rather infrequent finding in the diagnosis of herniated intervertebral disk. Nerve sleeve asymmetry or amputation sometimes is found.

Borrelli and Maglione believe that myelography should be performed in every case in which a lesion of the spinal canal is suspected in order to facilitate the surgical exploration by establishing the exact level and type of lesion. When the clinical evidence is controversial, they believe myelography to be a decisive diagnostic factor. The overall accuracy of diagnosis in their 150 cases was calculated to be 88%.

WEILAND, Grove City, Pa.

ROENTGEN DIAGNOSIS OF HERNIATED DISK WITH PARTICULAR REFERENCE TO DISKOGRAPHY (NUCLEOGRAPHY). W. G. PEACHER and R. P. STORRS, Am. J. Roentgenol. 76:290 (Aug.) 1956.

Peacher and Storrs review and discuss the existing literature concerning myelography and diskography in the diagnosis of the herniated intervertebral disk and illustrate the discussion with a few examples of lumbar diskograms taken from their own practice.

Advantages of lumbar myelograms are as follows: 1. Visualization of the entire spinal canal may be obtained. 2. The study is useful in differential diagnosis, for other lesions in the spinal canal besides herniated intervertebral disks can be identified and often diagnosed accurately. 3. Lesions which threaten compression of the spinal cord can be recognized early. 4. The study is accurate for the majority of the cases of herniated intervertebral disk. Disadvantages of lumbar myelograms as follows 1. A foreign material must be introduced into the subarachnoid space by lumbar puncture. This material may cause chemical arachnoiditis, is sometimes difficult to remove completely, and is absorbed slowly. 2. The procedure gives a small percentage of false-positive and false-negative results in the diagnosis of herniated intervertebral disk.

Advantages of diskography are as follows: 1. The contrast material need not be removed, is completely absorbed by the body, and is not used in the subarachnoid space. 2. Morbidity following the procedure is low. 3. The percentage of error is small. 4. The study provides a good deal of anatomic information concerning the disks which are studied, rather than just information concerning whether or not a posterior herniation exists. Disadvantages of diskography are as follows: 1. Although diskography can be used on any intervertebral disk if a high degree of technical skill is attained by the operator, for most practical purposes the procedure is limited now to the lowest three lumbar interspaces. 2. It has no value in the diagnosis of disease of any structure except the intervertebral disk. 3. Both false-negative and false-positive results can occur in the diagnosis of herniated disk. 4. Multiple lumbar punctures are required. 5. The examination is time-consuming, and considerable skill and experience are necessary to conduct it properly and to interpret the films which are obtained.

It is generally agreed that the degree of pressure necessary for injection, the amount of contrast material which can be injected, and the presence or absence of symptoms during the injection are all important diagnostic criteria and must be given weight in the final diagnosis, along with the appearance of the roentgenograms. Peacher and Storrs prefer to initiate the patient's roentgenographic investigation with a lumbar myelogram, since most patients with a strongly suggestive clinical history and positive physical findings of herniated disk will show positive myelographic results. Diskograms are recommended for those patients with suggestive histories but negative or equivocal myelograms, for those with atypical histories or negative or minimal neurological findings, and for those who have been treated without success.

WEILAND, Grove City, Pa.

ESTIMATION OF SKULL CAPACITY FROM ROENTGENOLOGIC MEASUREMENTS. I. L. MACKINNON, J. A. KENNEDY, and T. V. DAVIES, Am. J. Roentgenol. 76:303 (Aug.) 1956.

In a previous publication MacKinnon described how he measured the volume of 52 dry adult human skulls by pouring measured amounts of small lead shot into them until they were filled. MacKinnon and his associates now have made roentgenograms of these 52 skulls in the lateral and anteroposterior positions. The lateral roentgenograms were made with a perforated metal ruler marked in centimeters suspended over the film at the same level as the midsagittal diameter of the skull. When the anteroposterior films were made, the ruler was suspended over the film at the level of the widest part of the skull. Thus, the image of the ruler on the films can be depended upon to measure accurately any diameter drawn in the midline on the lateral roentgenogram and any diameter drawn at the widest portion of the skull in the anteroposterior roentgenogram.

Three internal diameters of the skull were measured on the lateral roentgenogram: (1) the length (L), the maximum internal anteroposterior diameter; (2) the height (H), measured from a point midway between the images of the external auditory meati to the farthest point located on the inside of the vault of the skull; (3) a diameter labeled B, measured from the interior of the skull at the bregma to the inside of the skull in the posterior cranial fossa; (4) a diameter, the internal width (W), measured on the anteroposterior view at the widest portion of the cranial cavity.

After all of these linear and volume measurements were made and tabulated, the relationship between each linear measurement and the actual volume of the skulls was determined, as well as the relationship between various combinations of linear measurements and the actual volume. It was found that if the length (L) diameter was multiplied by the number 84.2 the results would be a fair approximation of the volume of the skull, in cubic centimeters. The average error in this case was 6.7%, but the largest error in estimating the volume of any one skull in the group was found to be 18.2%. Comparable results were obtained if any other single diameter was used to estimate skull capacity. If the product of L×B×W was multiplied by 0.47, the result was the skull capacity, with an average error of only 3.5% and a maximum error of 8.72%. Of the product of L×H×W was multiplied by 0.57, the result was the estimated skull capacity with an average error of 3.0% and a maximum error of 7.7%. The sum of two products —0.255 (L×H×W) plus 0.255 (L×B×W)—resulted in an estimated skull capacity with an average error of 2.4% and a maximum error of 6.18%. It is suggested that a reasonable estimate of the capacity of any adult skull can be obtained from the four internal

roentgenologic diameters here listed, using the formula 0.255 (L×H×W) plus 0.255 (L×B×W).

WEILAND, Grove City, Pa.

FIBROUS DYSPLASIA OF THE SKULL WITH SARCOMA. A. A. HOBBS JR., W. C. FISHER, and R. E. BECK, Am. J. Roentgenol. 76:320 (Aug.) 1956.

Fibrous dysplasia does not commonly involve the bones of the cranium or face, and it is rarely complicated by malignancy. Cases of cranial fibrous dysplasia appearing in the medical literature are often called "leontiasis ossea," a purely descriptive term, which has also been used to describe the appearance of the head and face when these structures are involved with osteitis deformans, rickets, and endocrine disorders.

Hobbs and his associates report the case of a man who was first seen because of a painful swelling which had developed over his right eye after trauma three weeks before. Since adolescence he had been a very large man, with big hands and feet, a large head, and prominent features. Because of his physical appearance he had been an object of ridicule by village children. Roentgenograms of the skull showed heavy bone density in the right sphenoid, ethmoid, malar, frontal, and maxillary bones and in the right half of the mandible. In the right frontal region the diploic bone was uneven and had an appearance suggesting multiple cystic areas of various sizes within the bone. Fibrosarcoma was found in a biopsy taken from the bone in the swollen right frontal area. X-ray therapy produced regression of symptoms, but the patient died eight months later as a result of spread of the tumor.

WEILAND, Grove City, Pa.

GRANULAR CELL TUMOR OF THE NEUROHYPOPHYSIS. N. GLAZER, H. HAUSER, and H. SLADE, Am. J. Roentgenol. 76:324 (Aug.) 1956.

Granular-cell myoblastoma is a rare tumor arising in the hypophyseal stalk. It is thought most likely to arise from the neural, perineural, or endoneural cells. The tumor expands slowly and frequently attains considerable size. Visual impairment, caused by compression of the optic nerves, is a predominant symptom. Evidence of increased intracranial pressure eventually occurs.

Glazer, Hauser, and Slade report the case of a woman, 31 years old, who was seen because she had been blind for a month. The only abnormal finding of the physical examination was bilateral optic atrophy. Plain roentgenograms of the skull showed erosion of the dorsum sellae and the posterior clinoid processes. A pneumoencephalogram revealed elevation of the floors of the third ventricle and the right lateral ventricle. The tumor could be excised only partially. Deep X-ray therapy was given after operation, but the patient died during the course of treatments.

WEILAND, Grove City, Pa.

ROENTGENOGRAPHIC FINDINGS IN TRIGEMINAL NEURALGIA. W. J. GARDNER, E. M. TODD, and J. P. PINTO, Am. J. Roentgenol. 76:346 (Aug.) 1956.

The authors believe, as Taarnhøj did, that trigeminal neuralgia is caused by pressure on the sensory root of the fifth cranial nerve where it crosses the apex of the petrous bone. It is their theory that compression of this nerve root may occur as a result of upward displacement of the petrous apex which accompanies basilar impression. Osteoporosis occurs frequently in women after the menopause. Basilar impression is thought sometimes to be associated with osteoporosis, and thus might be expected to be found more frequently in older women. Trigeminal neuralgia is also found most frequently in older women. Therefore, there is probably a cause-and-effect relationship between basilar impression and trigeminal neuralgia. The authors tabulate roentgenographic findings on a series of 130 patients with trigeminal neuralgia and on another series of 200 "normals"—younger people with suspected intracranial lesions who did not have symptoms of trigeminal neuralgia.

Roentgenograms were made in the posteroanterior projection so that the images of the petrous pyramids would be projected through the orbits, where they could be well seen. The point at which the sensory root of the fifth nerve crosses the apex of the petrous pyramid was estimated, and the distance between this point and the top of the orbit on the same side was measured on the film. On the lateral roentgenogram, McGregor's line from the posterior end of the hard palate to the lowest portion of the

occipital bone was drawn, and the position of the odontoid process of the second cervical vertebra in relation to this line was determined. Using standards previously set up by McGregor, 43% of the cases of trigeminal neuralgia were thought to show evidence of basilar impression. However, 23% of the cases used as normal controls also were found to have basilar impression when judged by the same standard. The measurements which were made, the ages of the patients, and the presence or absence of trigeminal neuralgia were collected in the form of tables which pointed out relationships of two or more variables. From these tables it was concluded that (1) the right petrous apex is usually higher than the left in normals and in abnormals; (2) the basilar impression is more frequent in people who suffer from trigeminal neuralgia; (3) trigeminal neuralgia is commoner in women and is commoner on the right side; (4) trigeminal neuralgia is three times as common on the side of the higher petrous bone as it is on the side of the lower petrous bone; (5) in women with trigeminal neuralgia the odontoid process shows more upward displacement in older age groups than in younger age groups.

WEILAND, Grove City, Pa.

IMPROVEMENT OF OSSEOUS CHANGES IN THE SELLA TURCICA FOLLOWING IRRADIATION FOR A PITUITARY TUMOR. H. ADLER and G. KAPLAN, Radiology 66:856 (June) 1956.

Adler and Kaplan report the case of a 46-year-old white man who complained of enlargement of the head, jaw, hands, and feet; severe frontal headaches; numbness of the fingers; impaired visual acuity; drooping of the left upper eye; urinary frequency, and cachexia. The symptoms were slowly progressive over a period of eight years. Physical examination demonstrated acromegalic changes involving the bones of the skull, face, hands, and feet; dilatation of the left pupil, which did not react to light; loss of lateral movements of the left eye and weakness of the left ocular movements, and contraction of the visual fields of both eyes.

Roentgen examination of the skull demonstrated prognathism, enlarged frontal sinuses, considerable enlargement of the sella turcica, and thinning of the dorsum sellae and posterior clinoid processes. It was thought that the patient probably had a combined eosinophilic and chromophobe adenoma of the pituitary gland. He was given deep x-ray therapy and received an estimated tumor dose of 3000 r in a period of four weeks. After treatment the patient improved subjectively and objectively. His visual acuity improved. Examination of the visual fields showed marked improvement bilaterally. All symptoms of cranial-nerve abnormality disappeared. Roentgenograms of the skull made a year and a half later showed that the dorsum sellae had become considerably smaller than it was before, and the floor of the sella, the posterior clinoid processes, and the dorsum sellae appeared to have normal thickness.

WEILAND, Grove City, Pa.

Books

Der Neurogene Nystagmus. By Johannes Ohm. Price, not given. Pp. 134. Ferdinand Enke, Hasenbergsteige 3, (14a) Stuttgart, W., 1955.

This book represents the summary of the author's theories and experiences with nystagmus, based mainly upon working with the problems of miner's nystagmus.

The author lists and discusses the conventional types of nystagmus and emphasizes the necessity of recording nystagmus. He discusses the limitations of the various methods in use and points out the advantages of his method, the lever system. From the recorded graph, the author is able to deduct formulas analogous to Ohm's Law, giving quotients analogous to the energy quotients, which he believes help characterize the various types of nystagmus, such as optokinetic, vestibular, and miner's.

He uses graphs, tables, and case histories as illustration. The author believes that the "center" responsible for the development of nystagmus is the vestibular nuclear complex (divided into right and left vertical, horizontal and rotatory nystagmus centers), receiving impulses from the cerebral cortex and the sensory organs (eye, labyrinth, neck muscles, etc.) and reacting upon eye muscles. The methods used for evaluating and recording nystagmus are interesting from the point of methodology, but they do not appear to be generally applicable to clinical work.

The Organization of the Cerebral Cortex. By D. A. Sholl. Price, 18s; $4.25. Pp. 140. Methuen & Co., Ltd., 36 Essex St., Strand, London, W. C. 2; 440 Fourth Ave., New York, 1956.

This excellent small volume, by an English anatomist, consists of two sections. The first is a well-organized, concise statement of histological methods and observations that are likely to be important for the "mode of operation of the cerebral cortex." This section includes data concerning the total extent of the cortex, total number of neurons in the cortex, density of neuronal packing in the cortex, etc. These portions are well done and are accompanied by illustrations showing beautiful preparations of brain sections. A chapter is devoted to a discussion of the qualitative histology of the cerebral cortex; the author joins a distinguished group of predecessors in rejecting a cytoarchitechtonic basis for conceptions of the cortex as an aggregate of organs each with its special function.

The second section is an essay touching briefly on a number of conceptual models of cerebral function. Here the author's hand is less sure. However, the span of the studies covered in this essay is broad, and the writer is brief; there is virtue in having so many aspects of the current scene touched on in a single volume.

In his conclusions, the author takes part in a rising tide against the search for correlations between such concepts as "memory" and "intelligence" and the activity of circumscribed regions of the cortex. He states: "Experimental work has shown little evidence for regional specialization of this kind and one is driven to the opinion that these properties are general attributes of all cortical tissue." Discussion of mathematical and electronic models of brain mechanisms follows. As a final conclusion, the goal of investigations of the organization of the cerebral cortex is cited as being the construction of "a deductive system in which observable consequences follow logically from the conjunction of observed facts with the fundamental hypotheses of the system." This model should be "based on the concept of probability and discussed in statistical language." To one accustomed to the biological laboratory and the troubles of persons with injured brains, the language of such goals seems alien and somehow beside the point.

L. Chapman.

Neurochemistry. By S. R. Korey and J. Nurnberger, Editors. Vol. I. Price, $6.75. Pp. 244. Paul B. Hoeber, Inc. (Medical Book Department of Harper & Brothers), 49 E. 33d St., New York 16, 1956.

This volume is the first of a planned series entitled "Progress in Neurobiology." Sixteen chapters, varying in length from 8 to 29 pages, are presented by a total of 22 contributors.

The chapters are arranged in the form of journal papers or short reviews, and present the authors' experimental results and discussions of work concerned either directly or indirectly with the structure, composition, and metabolism of nerve tissue. Topics covered vary widely. They include chemical studies of sphingosines, acetal phospholipids, brain copper proteins, and nucleic acids; enzymatic studies of thioltransacetylation, metabolism of γ-amino-butyric acid, adaptation in chick embryos, and changes during brain development; electron microscope studies of the neuron; metabolic studies of normal and epileptogenic human brain; relation of copper and ceruloplasmin to Wilson's disease; effect of cold stress on nitrogenous components of brain; production of allergic encephalomyelitis by brain lipoproteins; effects of drugs on nerve conduction, and cerebral blood flow and oxygen consumption in relation to mental activity, age, mental retardation, and epilepsy.

The principal value of the book lies not in providing a comprehensive and integrated picture of present-day knowledge of neurochemistry, but in delineating some of the unsolved problems in this field and in illustrating experimental methods of attack. One of the desirable features of progress reports of this type is that they be as up-to-date as possible. A cursory scanning of the 470 literature references given in the various chapters revealed only 5 for 1955, the latest year included. No discussion of serotonin or related material is given. In spite of these drawbacks, the book is of value in providing interesting, and frequently stimulating, discussions of selected topics in neurochemistry by experts in the field.

News and Comment

ANNOUNCEMENTS

International Poliomyelitis Congress.—The Fourth International Poliomyelitis Congress will be held at Geneva, Switzerland, July 8-12, 1957. For information, write International Poliomyelitis Congress, 120 Broadway, New York 5.

GENERAL NEWS

Responsibilities of the Medical Profession in the Use of X-Rays and Other Ionizing Radiation: Statement by the United Nations Scientific Committee on the Effects of Atomic Radiation.—The United Nations General Assembly, being aware of the problems in public health that are created by the development of atomic energy, established a Scientific Committee on the Effects of Atomic Radiation. This Committee has considered that one of its most urgent tasks was to collect as much information as possible on the amount of radiation to which man is exposed today, and on the effects of this radiation. Since it has become evident that radiation due to diagnostic radiology and to radiotherapy constitutes a substantial proportion of the total radiation received by the human race, the Committee considers it desirable to draw attention to information that has been obtained on this subject.

Information received so far indicates that, in certain countries (Sweden, United Kingdom, United States of America), by far the most important artificial source of such radiation is the use of radiological methods of diagnosis and that this may be equal in importance to radiation from all natural sources. It is possible that such radiation may be having a significant genetic effect on the population as a whole.

It appears most important, therefore, that medical irradiations of any form should be restricted to those which are of value and importance, either in investigation or in treatment, so that the irradiation of the population may be minimized without any impairment of the efficient medical use of radiation.

The Scientific Committee on the Effects of Atomic Radiation established by the United Nations General Assembly accepts the view that the irradiation of human beings, and especially of their germinal tissue, has certain undesirable effects.

The Committee is fully aware of the importance and value of the medical use of radiations but wishes to draw the attention of the medical profession to these facts and to the need for a more accurate estimate of the amount of exposure from this source. The help of the medical profession would be most valuable to make it possible to obtain fuller information on this subject.

Postpartum Mental Illness

A Controlled Study

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Mental illnesses associated with pregnancy and childbirth have been the subject of many studies in the last 25 years. Because of divergent criteria and definitions, few of these studies have been comparable. Major sources of confusion have been the lack of a proper definition of a postpartum mental illness, whether there is a specific psychosis occurring in the postpartum state, and to what extent the common factor, childbearing, influences the course. There has been a notable lack of control groups in previous studies, so that the postpartum patient was viewed without benefit of comparison with a comparable patient group. Adequate follow-up studies have been lacking, and there has been confusion about the role of toxicity in producing this illness.

Design

The present investigation was undertaken in an attempt to clarify various aspects of definition, incidence, pathology, dynamics, and prognosis of the postpartum mental illness. Its purpose is essentially an exploratory one, that is, to investigate a group of patients whose mental illness had been precipitated by childbirth. The term "postpartum illness" is defined in this study to mean any mental illness in a female patient in which childbirth is a major precipitating factor, independent of the time of onset. The mental illness might start during pregnancy or after delivery, as long as childbirth itself seemed to set off the illness. No patient is included in this study who required hospitalization for mental illness during pregnancy. This group of patients, hereinafter referred to as the experimental group, was compared with a control group of patients whose illness had not been precipitated by childbirth. The experimental group consisted of 100 female patients admitted to the New York Hospital—Westchester Division between 1944 and 1952 for a mental illness which was judged to be precipitated by childbirth. (Mental illness precipitated by an abortion or by adoption was excluded.) The control group consisted of 100 female patients admitted to this same hospital and who were matched for age, and for year of admission, but in whom childbirth was not a precipitating factor. The mean age of the experimental group was 30.6 years, with a range of 19 to 43 years; the mean age for the control group was 30.7 years, with a range of 19 to 44 years. The point of observation was in a mental hospital where these patients were in residential psychiatric treatment for their mental illness. A thorough follow-up study was an integral part of the experimental plan.

Submitted for publication Nov. 26, 1956.

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Read at the Second Divisional Meeting of the American Psychiatric Association, Montreal, Canada, Nov. 9, 1956.

Descriptive Characteristics

Diagnosis.—Table 1 compares the psychiatric diagnoses for the experimental and control groups. The diagnoses used were arrived at in staff conference held after the patient had been in the hospital for at least two months. The χ^2 test was applied to the larger categories, 1 through 4, that appear in Table 1, revealing the results to be sig-

TABLE 1.—*Diagnoses of Postpartum Group Compared with Control Group*

Category	Postpartum Group	Control Group
1 Psychoneurosis		
Mixed	15	12
Reactive depression	5	1
Anxiety state	1	2
	21	15
2 Dementia praecox		
Catatonic	29	27
Paranoid	15	17
Simple	3	1
Hebephrenic	2	3
Other types, depressed	1	1
	50	49
3 Manic-depressive illness		
Depressed	8	6
Mixed	6	6
Manic	5	3
Circular	5	7
Perplexed	1	1
	25	23
4 Other		
Paranoid condition	1	2
Psychosis with psychopathic personality		
Episode of excitement	1	3
Episode of depression	0	2
Without mental disorder		
Alcoholism	1	1
Drug addiction	1	2
Psychosis due to alcoholism, delirium tremens	0	1
Involutional psychosis, paranoid type	0	1
Psychopathic personality, asocial and amoral trends	0	1
	4	13
Totals	100	100

nificantly different at the 0.05 level. (Where statistical comparisons have been made, the χ^2 has been used. In this technique P must equal 0.05, or preferably 0.01, for the results to be considered significant, indicating that the probability is 5 in 100, or 1 in 100, that the results are due to chance alone.

It is apparent, then, that the postpartum illness, as defined in this study, resulted in different psychiatric diagnoses than did mental illness not precipitated by childbirth. However, this finding cannot be taken at its face value. A closer examination of Table 1 will explain the difference. There is no significant difference between the experimental and the control group as regards psychoneurosis, dementia praecox, or manic-depressive illnesses, as measured by the χ^2 technique. The significant difference occurs in Category 4, "Other." Postpartum patients did not contain as many alcoholic and drug diagnoses as did the control group, or as many psychopaths. A possible explanation of this finding is that psychopaths may be less likely to have marriages resulting in childbirth, and patients with alcoholism and drug addiction usually show long-standing maladjustment which has interfered with marriage and the normal production of children. Therefore, the differences in psychiatric diagnoses, although statistically significant, are not interpreted as a basic difference in mental reaction to childbirth, but represent only a difference in life adjustment which would probably exclude certain types of patients from experiencing marriage resulting in childbirth.

The significant point is that dementia praecox, and the manic-depressive illnesses, as well as the psychoneuroses, occur with the same frequency in the postpartum setting as they do in any other setting. These findings regarding diagnosis differ from those of other authors, and this may be due to the change in the diagnostic frame of reference over a period of years. For example, Smalldon[1] found at this hospital, in 1940, almost the reverse proportion between dementia praecox and the manic-depressive illnesses than that which appears in

this experimental group. This probably reflects a change in the diagnostic pattern in the past 15 years. In some of the earlier articles, many diagnoses included toxic reactions, which are far less common today. In 1943 Jacobs [2] found almost 50% of his group in the manic-depressive category, as had Smalldon, and assigned about 30% to a mixture of delirium and catatonic symptomatology. The results of the present study are the reverse, with 50% of the experimental group in the dementia praecox (or schizophrenic) category, approximately 25% in the manic-depressive group, and another 25% in the psychoneurotic group. Cruickshank [3] was another worker who emphasized the toxic-exhaustive psychoses, which do not appear in the present group. Even Boyd [4] included the delirium reactions in his diagnoses. What has probably happened is that those illnesses formerly considered as toxic or exhaustive processes are now considered dementia praecox, for which reason the proportion of such diagnoses has increased. Regardless of historical changes in diagnoses, the important question is whether postpartum patients differ diagnostically from a concurrent control group when the same criteria are applied to the presenting symptomatology. This question is answered in this study in the negative, if one excludes the various psychopathic and addict categories.

The question of age may be relevant to diagnosis. The mean age of the postpartum group was 30.6 years, and the control group was matched for age. This age is a little higher than has been reported by other workers, such as Cruickshank,[3] Jacobs,[2] and Smalldon,[1] whereas it is in agreement with that given by Skottowe.[5] It is the age group in which schizophrenia is a common diagnosis.

In relation to diagnosis, the early symptoms of mental illness in a postpartum patient become significant. Obviously, the psychiatric symptoms exhibited by these postpartum patients would be those found in dementia praecox, the manic-depressive illnesses, and the psychoneuroses. Symptoms included depression, excitement, delusions, tension, anxiety, hallucinations, etc. Other authors, Karnosh [6] and Linn,[7] seem to have emphasized the excitement and delusions that occur in the postpartum illness, to the exclusion of the neurotic symptoms and the very frequent depressions, which comprise nearly half of the cases in this study. If one hoped to recognize a postpartum illness only by symptoms of excitement and confusion, the psychoneurotic and many of the manic-depressive patients would be overlooked.

Religion

Two authors, Smalldon [1] and Strecker,[8] have noted a high frequency of patients of the Jewish faith among the postpartum groups studied. For that reason, a comparison was made of the religious affiliations between the experimental and the control groups (Table 2). These differences were not significant, and therefore the conclusion is reached that no one religious group produces proportionately more postpartum illness than does any other. Many of the previous studies failed to take sampling problems into account, or did not compare the postpartum patients with other patients admitted to the same hospital at the same time, and consequently such statements were not necessarily valid.

Previous Illness.—There has been considerable speculation as to whether or not the postpartum illness constitutes a psychiatric entity by itself. The implication has been that postpartum illness occurs in patients who otherwise might not have had a mental illness. It was appropriate, therefore, to compare the number of previous episodes of mental illness and the number of previous hospitalizations of the postpartum group with those of the control group. The comparison appears in Table 3. This information was compiled at the time of admission for both groups. (It must be

TABLE 2.—*Religious Affiliation of Postpartum Group Compared with Control Group*

Religious Affiliation		Postpartum Group		Control Group
Protestant		49		56
Hebrew		25		18
Roman Catholic		23		20
Other		3		6
Christian Science	1		2	
Fundamentalist	2		1	
Greek Orthodox	0		1	
No religion	0		2	
Total		100		100

remembered that not all previous episodes required hospitalization, and that there could be more than one hospitalization for any one episode.) There was no statistically significant difference between the number of previous attacks or between admissions for the two groups. It would be correct to assume, then, that these two groups were derived from the same theoretical population as regards previous mental illness. Moreover, it cannot be held that the postpartum illness occurs in patients without previous mental difficulty. The postpartum patient is like any other female patient of the same age admitted to this hospital in respect to previous mental instability. Approximately 30% of both the postpartum group and the control group had suffered a previous attack of mental illness prior to this hospitalization, and between 20% and 30% of both groups had suffered a previous admission to a mental hospital. (Approximately two-thirds of both groups were experiencing their first known overt attack of mental illness.) These similarities would support the theory that the postpartum illness is not a unique illness nor one that happens to otherwise healthy subjects who merely react abnormally to motherhood.

Duration of Onset.—It was thought possible that the length of onset of the illness, prior to this hospitalization, would differentiate these two groups, even though the number of previous attacks and of hospitalization did not. This proved to be true, with a mean onset of 13.9 months for the postpartum group, as compared with 19.0 months for the control group, this difference being significant at the 0.01 level. The postpartum group obviously had a shorter onset. It is presumed that the control group contained more patients who showed chronic maladjustment or an insidious onset.

Duration of Hospitalization.—Although the postpartum patients had as much previous mental illness as had the controls, they showed a shorter onset. This raises the question: Would the shorter onset correlate with a shorter period of hospitalization? Hospitalization is defined here as the period of time spent in the New York Hospital—Westchester Division and does not refer

TABLE 3.—*Previous Mental Illness of Postpartum Group Compared with Control Group*

No. of Previous Attacks	Postpartum Group	Control Group
None	68	66
One	25	18
Two	4	9
Three	3	4
Four or more	0	3
	100	100

No. of Previous Admissions	Postpartum Group	Control Group
None	79	69
One	15	21
Two	6	5
Three	0	3
Four or more	0	2
	100	100

to any subsequent hospitalization or transfer to any other hospital. Length of hospitalization in this hospital does not necessarily reflect the amount of improvement, since hospitalization may be terminated against the advice of the medical staff. This often meant that relatives removed the patient from the hospital at the first sign of improvement or of a better adjustment, although the senior staff felt this level of recovery was not adequate for a return home. The results of this comparison showed that the postpartum group did have a shorter hospitalization, which difference, again, was significant at the 0.01 level. The postpartum patient spent a mean of seven months in this hospital, as compared with a mean of eight months for the controls.

Condition at Discharge.—Since the postpartum group had a shorter onset and a shorter hospitalization, one might wonder whether these patients were discharged at a better level than was the control group. The comparison was made between the two groups for the level of discharge. Approximately the same number (21 and 23) were discharged as "unimproved"; the exact same number (34) had "recovered," but 30 controls were discharged as "much improved," as compared with only 17 of the postpartum group. These differences prove significant at the 0.02 level. The control group, therefore, was discharged at a better level of adjustment than was the postpartum group.

Type of Discharge.—The postpartum group stayed in the hospital for a shorter period but showed a poorer level of recovery at time of discharge than did the controls. This was partly due to the type of discharge. An unduly high proportion of the postpartum patients left the hospital "against advice." This means that in the opinion of the hospital staff they were not in condition to leave, and none of these patients were considered "recovered." One-third of all the postpartum patients left the hospital "against advice," whereas only 15% of the control group were so discharged. This difference is significant at the 0.01 level. The 33 patients who left the hospital "against advice" were discharged sooner than was deemed advisable, for their average length of stay was only 4.4 months, as compared with 7 months for the total postpartum group. There are many reasons why relatives press for early discharge of a postpartum patient, the most obvious being the need to care for the infant. It was necessary to undertake the follow-up study in order to determine whether or not this group did as well on the whole as did the other postpartum patients.

Eventual Outcome.—In order to do a thorough follow-up study of these 100 postpartum patients, a questionnaire was sent to close relatives who were in a position to provide recent and accurate information as to the patient's adjustment in the community. The time interval from discharge to follow-up ranged from 8 to 118 months, with a mean time lapse of 47 months. Over four letters per patient were required to obtain sufficient information, and telephone calls were employed where necessary.

In the follow-up questionnaire, seven major areas were covered to elicit information regarding the patient's adjustment. These seven areas were physical health, change in marital status, additional children and reaction to these pregnancies, further psychiatric treatment, employment, special difficulties, and present level of adjustment. Additional information, including examples and anecdotal reports, were frequently volunteered on the replies. For those who had subsequent periods of hospitalization or extramural psychiatric attention, additional information was obtained by letter from such sources.

The returned questionnaires from relatives, physicians, and hospitals, as well as the data acquired verbally, were collated for each postpartum patient. These data were then examined by three of us and a joint decision reached as to the proper category of adjustment. Ten categories were

chosen for this scale of increasing dysfunction, the step intervals of which are not precisely equidistant, but are graduated. The scale of adjustment was as follows:

1. At home, apparently recovered, full- or part-time outside employment
2. At home, apparently recovered, not employed
3. At home, level of adjustment considered fair
4. At home, marginal adjustment
5. At home following psychosurgery
6. Still in hospital
7. Still in hospital following psychosurgery
8. Suicided.
9. Deceased, cause unknown
10. No report

"Apparently recovered" meant the patient was reported to be at home, adequately meeting her responsibilities and not considered in need of further psychiatric treatment. "A fair adjustment" was assigned to those cases in which there were certain reservations, such as "good but still in treatment," "extremely well, but high-strung," "fairly adequate," "having change of life and is occasionally nervous and irritable; otherwise seems normal." "Marginal adjustment" was indicated by poor functioning at home and the presence of interfering symptoms. This group may or may not have been in outpatient treatment. Typical replies assigned to this category were as follows: "Upset a year ago, suicidal"; "she feels she has one foot in the grave and one on a banana peel"; "had psychotherapy and further shock treatment with negative results; still has obsessive neurosis." To Category 5, "at home, following psychosurgery," were assigned those patients who had undergone lobotomy, topectomy, or similar surgical procedures. Their adjustment level most closely approximated those of the marginal adjustment group. One such patient was described as having poor sleeping habits, need for sedation, nervous tension, and obsessional thinking. A relative reported: "Her present state is a sort of in-between stage; she is neither very emotionally ill, nor is she well." "Still in hospital" and "still in hospital following psychosurgery" refer to any psychiatric hospital in which the patient was resident at the time of follow-up but does not necessarily imply one continuous hospitalization. The remaining three categories—"suicided"; "deceased, cause unknown," and "no report"—are self-explanatory.

Table 4 summarizes the follow-up data. Fifty-seven postpartum patients achieved apparent recovery, as designated by either Category 1 or Category 2. An additional 15 patients have made a fair adjustment. Eleven patients were reported at the marginal level of adjustment, as represented by Categories 4 and 5, but were still able to remain out of the hospital. An additional 11 patients, 4 of whom have undergone psychosurgery, are still hospitalized. Thus, 11% of the experimental group could be regarded as the chronic and unimproved group. Of the six remaining patients, three have suicided, and one was reported as deceased, cause unspecified, after having had additional hospitalization and further outpatient treatment. Sufficient information was not obtained to rate the adjustment of the remaining two patients. In summary, then, 57% of the experimental group achieved an apparent recovery, and an addi-

TABLE 4.—*Adjustment Level of Postpartum Group as Ascertained by Follow-Up Study*

Category	Left Hospital with Approval	Left Against Advice	Total
1. At home, apparently recovered, full or part-time outside employment	16	4	20
2. At home, apparently recovered, not employed	25	12	37
3. At home, level of adjustment fair	9	6	15
4. At home, marginal adjustment	5	4	9
5. At home, following psychosurgery	0	2	2
6. Still in hospital	5	2	7
7. Still in hospital, following psychosurgery	3	1	4
8. Suicided	3	0	3
9. Deceased, cause unknown	0	1	1
10. No report	1	1	2
	67	33	100

tional 15% achieved a fair level of adjustment. If these two groups are combined, 72% of the experimental group can be said to have achieved a reasonable level of adjustment some four years after hospitalization.

One would wonder whether or not the diagnosis of the patient correlated in any way with the eventual outcome. A comparison was made of diagnosis and prognosis, and the results were not significant. Therefore, it cannot be said that postpartum patients who were diagnosed as schizophrenic do less well than those with other diagnoses, a finding which is contrary to those of other writers, such as Boyd [4] or Skottowe.[5] This difference may be due to a change in the diagnostic frame of reference, to electroshock therapy, or to the observation that patients are entering the hospital earlier in their illness than they did formerly. These optimistic follow-up results seem to contradict the poor prognosis given in many other studies. However, the follow-up period averaged four years, which was considerably longer than has been used by many other writers, and the detailed reports were judged against specific criteria. These optimistic results can, therefore, be judged as conservative and would suggest that three out of four postpartum patients, such as have been studied here, could expect to be at a reasonable level of recovery some four years after their hospitalization.

It is difficult to compare these results with those of other studies of mental illness because of differences in population, stage of illness, or method of study. The ideal comparison for follow-up purposes would have been an identical follow-up study for the 100 control patients. But such an undertaking was beyond the scope of this study. A partial comparison can be made with another study from this hospital by Hamilton and Wall,[9] whose subjects were from the same population and who were admitted between 1942 and 1946. This study concerned 100 consecutive female schizophrenic admissions whose average age was 28 years, only 2 years younger than that of the postpartum group. Almost half were married, and about one-third had children. Follow-up results for these schizophrenic patients, made from one to six years after hospitalization, revealed 33 recovered, 24 improved at home, and the balance, 33, not improved. The postpartum group as a whole did a great deal better than this, with 57 recovered, 26 improved (if Categories 3, 4, and 5, from Table 4, are grouped together for purposes of comparison), and 11 not improved. The difference in adjustment between these two groups was significant at the 0.01 level.

One might conclude from this comparison that the postpartum reaction has a better prognosis than a patient with a schizophrenic illness from a comparable population. But when the schizophrenic patients were compared with the 50 postpartum patients who were also diagnosed as schizophrenic, the results on the follow-up were not statistically different. The only valid conclusion from these data, then, is that schizophrenic postpartum patients have the same prognosis as do nonpostpartum schizophrenics. The fact that the postpartum group cut across diagnostic lines and included illnesses with a generally more favorable immediate prognosis than schizophrenia, such as psychoneurosis and the manic-depressive disorders, probably accounts for the better prognosis in the postpartum group than in a solely schizophrenic one. That postpartum schizophrenics have a prognosis about equal to that of nonpostpartum schizophrenics is at variance with the results of Brew's study,[10] where the prognosis was poorer for the postpartum group. Smalldon [1] found, on the other hand, that prognosis in the postpartum schizophrenic group was better than in other groups. There have been two other studies of prognosis for the postpartum illness that need comment here. One has been made by Zilboorg [11] to the effect that postpartum schizophrenics rarely, if ever, make any suicidal attempts. The data from this study

would contradict this statement, not only because one schizophrenic patient eventually succeeded in suiciding, but because, in many of these cases, suicidal attempts were reported. Second, Cruickshank [3] found a considerably lower level of eventual adjustment than was true of this present group, which may be due to the general prognosis for these illnesses some 15 years ago, before the advent of certain somatotherapies, and because of present earlier hospitalization.

The eventual adjustment of the 33 patients who left this hospital "against advice" showed a significantly lower level of adjustment upon follow-up than those who left with staff approval. This difference was significant at the 0.01 level. The conclusion would seem justified that leaving "against advice" was related to a poor prognosis and would argue against premature termination of hospitalization for this group.

Another interesting finding of the follow-up study was that 22 of the postpartum patients had a total of 27 additional pregnancies following discharge from this hospital. Only three of these patients subsequently suffered mental illnesses requiring hospitalization, and only one of these patients is presently in a hospital. Eighteen patients reacted to these pregnancies in a manner that was reported as "excellent" or "good." On the basis of this small sample, one would estimate the chance of a subsequent mental illness following another pregnancy as only one in seven for the individual postpartum patient, a figure which is considerably more optimistic than has been commonly held. Boyd,[4] for example, felt a very conservative policy was indicated for further pregnancies and that they should not be permitted if a schizophrenic psychosis had occurred. This statement is not borne out by the findings of this study, although the sample is small, but it does raise the question whether there has not been undue pessimism regarding future pregnancies.

To recapitulate, the follow-up portion of the study resulted in three major findings. First, patients who left the hospital "against advice" did not achieve as favorable a level of recovery as did those patients remaining until discharged with staff approval. Second, further pregnancies following a postpartum illness indicated that the chance existing in this sample of a second mental illness occurring in an individual patient following another pregnancy was only one in seven. Finally, and this is a most optimistic finding, the postpartum illness as a whole has a favorable prognosis. Nearly 60% of the experimental group are now home and considered recovered. Another 25% can be considered improved. Only 10% of this group was not improved upon follow-up, with the remaining 5% deceased or the outcome unknown. The chances for a complete recovery from the postpartum illness, based on this study, would be 6 in 10, with an additional 3 chances in 10 that the level of adjustment would be "improved."

One further point of information that we felt merited investigation was the determination of whether the postpartum illness was precipitated by the birth of the first or of a later child. As to the actual rank of the child whose birth seemed to precipitate the illness, 57 of the postpartum patients reacted to the birth of their first child, 26 to their second, 13 to their third, and 4 to their fourth. Obviously, the incidence would decrease with the rank of the child, since there is an inverse relationship in the population between the rank of a child and the number born. On the other hand, it can be said that almost one-half of these postpartum patients reacted to the birth of a later child rather than to that of their first, contrary to some common conceptions. Almost half of these patients had experienced childbirth at least once without a frank mental illness. This observation is in agreement with the findings of Cruickshank,[3] Linn,[7] and Smalldon.[1] Since almost one-half of the patients reacted patho-

logically to the birth of a second or of a later child, it is hard to see an objective connection between the experience of childbirth itself and the subsequent mental illness. We have not attempted to evaluate physiological change surrounding childbirth as a possible explanation for the postpartum illness. But it must be pointed out that at least one-third of these patients showed their first psychiatric symptoms well after leaving the maternity hospital, and probably after having left the care of their obstetrician. There is no pattern here to suggest a direct causal relationship among the toxemias of pregnancy, delivery, and the onset of the postpartum illness. A temporal relationship is obviously demonstrated, but it is a variable one.

This section, which has dealt with the descriptive characteristics of the postpartum experimental group, seems to answer the question whether or not the postpartum illness is a psychiatric entity. Since those patients whose mental illness was apparently precipitated by childbirth did not differ substantially from control groups as regards diagnosis, previous mental illness, or prognosis, the conclusion seems justified that the postpartum illness is not a psychiatric entity. Therefore, we cannot agree with Boyd[4] or Jacobs,[2] who felt that the postpartum illness is a special type of mental disorder. This conclusion may result from the way in which such patients have been studied, since we did not limit ourselves to any specific time interval, but studied all patients who were received at a mental hospital for a mental illness which was apparently precipitated by childbirth. The results might have been different had we chosen to study only those patients who became upset within a restricted time interval after childbirth. Such arbitrary time limits are open to question. The results of this study would not appear to justify terming the postpartum illness as a separate illness, any more than one might term those young patients who react unfavorably to college as sufferers from a "college psychosis." The temporal connection would be obvious in both cases, but as regards diagnosis and prognosis the postpartum group is not different from any other group of female patients admitted for mental illnesses occurring at the same age.

Conclusion

This study of postpartum patients has resulted in the following findings: 1. The postpartum illness is not a disease entity in itself. 2. No one religious group showed a stronger predilection for a postpartum illness than did any other group. 3. Almost one-half of these postpartum illnesses were in reaction to the birth of a second or a later child. 4. The postpartum patient was like any other female patient of the same age admitted to this hospital in respect to previous mental instability. 5. Schizophrenic postpartum patients had the same prognosis as do nonpostpartum schizophrenics. 6. Three out of four postpartum patients were found to be at a reasonable level of recovery some four years after their hospitalization. 7. The chance of a subsequent mental illness following another pregnancy was only one in seven for the postpartum patient in this sample. 8. The postpartum patient has a favorable prognosis.

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Neuropharmacologic Action of Rauwolfia Compounds and Its Psychodynamic Implications

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The introduction of Rauwolfia alkaloids as antihypertensive drugs and as tranquilizing agents has produced a tremendous surge of optimism, sometimes uncritical, in regard to their virtues. It also has stimulated neurophysiologic and neuropharmacologic research. The clinical effect of these drugs has not been thoroughly investigated in a psychodynamic sense, nor have these effects yet been sufficiently correlated with the modern neurophysiologic concepts that attempt to explain complex adaptive behavior. This paper attempts to review pertinent literature relative to the neuropharmacologic action of Rauwolfia compounds, to report observations in a series of cases in which their effects were adverse to adaptive behavior, and to present a speculative hypothesis to explain these effects. It is hoped that such an effort may be helpful as the neurophysiologist and the practitioner of psychodynamics struggle from opposite ends of a long tunnel, groping in the dark toward a meeting place where the problems of consciousness, arousal mechanisms, visceral brain functions, the unconscious, the defensive functions of the ego, and oral narcissistic needs can be understood with a common language.

General Background

The root of Rauwolfia serpentina, a shrub indigenous to India, has been employed for centuries in native Indian medicine for the relief of various derangements of the central nervous system, both psychic and motor, including anxiety, excitement, and maniacal behavior associated with psychoses.

In 1952 Müller and associates [1] reported isolation of a previously undetected alkaloid from the so-called oleoresins of Rauwolfia root. Bein [2] made the initial pharmacologic report on this alkaloid (reserpine) and showed that both central nervous system depressant and hypotensive actions were shared by the same substance. Clinical trials utilizing these actions on both hypertensive and psychiatric patients were started immediately and have been reported extensively. Research went forward concurrently concerning the mode of action of the drug.

Plummer and associates [3] established the fact that reserpine exerts a calming and sedative action in a wide variety of animal species and suggested that the observed effects were explicable on the basis of an alteration of sympathetic-parasympathetic balance by partial suppression of the sympathetic predominance at the hypothalamic level. They noted a latent period after administration before the effects became apparent. Schneider and co-workers [4] postulated that reserpine brings about an increase of cortical inhibition on diencephalic structures but did not illustrate specific pathways whereby this effect was mediated. They did conclude, however, that the cortex was necessary to produce the characteristic effect of reserpine in animals.

Rinaldi and Himwich [5] presented electroencephalographic evidence that reserpine has no depressant effect on the alerting mechanism and, indeed, may enhance it. These investigators, however, considered these effects from the point of view of a "meso-

Received for publication Jan. 7, 1957.

Read at the meeting of the American Psychosomatic Society, Boston, March 24 and 25, 1956.

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diencephalic activating system," which includes both the reticular formation of the brain-stem tegmentum of Moruzzi and Magoun and the diffuse thalamic projection system of Jasper. They did not mention the possibility that the drug might have a differential effect on the two systems. Magoun [6] stated that influences leading to desynchronization of the cortex and arousal may be transmitted to the cortex by way of an extrathalamic route from the subthalamus to the internal capsule, and also through nonspecific and possibly other thalamic nuclei that for the most part lie dorsal and lateral to the most excitable zone. Magoun also said that indirect connections are present through the dorsal and lateral portion to the nonspecific thalamic system and thence to the hippocampus; he gave evidence that this route requires more and longer stimulation to produce the same electric effect at the cortex. Domino [7] presented evidence that these two systems have biochemical and physiologic differences and react differently to ether (ethyl ether), barbiturates, and mephenesin. Rinaldi and Himwich [5] concluded that reserpine altered consciousness in some fashion, but not via a direct effect on the cortex or by a depressant effect on the brain-stem reticular system, and that its action was quite different from that of barbiturates.

Weiskrantz and Wilson [8] investigated the changes in behavior of monkeys in which lesions were created surgically in the amygdaloid nucleus and which received reserpine. They suggested that the effects of reserpine were indistinguishable by them from those brought about by ablation of a larger system, consisting of the prepyriform cortex, anterior insula, anterior temporal pole, and posterior orbital-frontal regions.

MacLean [9] discussed neuronographic and electroencephalographic evidence that this region of the cortex has afferent connections with the amygdaloid nucleus and rostral hippocampus and hippocampal gyrus, and thence has a heavy projection onto the hypothalamus, septal region, and parts of the basal ganglia. The diffuse thalamic projection system of Jasper and its cortical projection on the cingulate gyrus complete the system proposed by Papez; if reserpine exerts its action here, one could account for its unique effect on affective consciousness without a corresponding effect on ideational awareness.

Brodie and associates [10] recently presented evidence that reserpine has its neurochemical action as a competing antimetabolite for serotonin and from these data explained both the latent period noted after administration of reserpine and its gradually cumulative effect. As yet, differential concentrations of serotonin in various parts of the human brain have not been reported. However, it has not been found in peripheral nerves or in the cortex of animal brains. Serotonin increases in concentration in animal brains as the relative amount of cortex decreases, and it may be permissible to infer that serotonin is a phylogenetically ancient neurohumoral agent in the phylogenetically oldest part of the higher integrating system, namely, the rhinencephalon. The validity of this inference must await direct spectrofluorometric measurement.

Schneider's group [4] presented evidence that the effects of reserpine on the nervous system are widespread if the drug is given in large single doses but are much narrower in action if it is used in amounts comparable to the clinical dose. This, together with the aforementioned observation of Magoun that longer and greater stimulation is necessary in the nonspecific thalamic system in order to produce similar cortical effects, and the neuropharmacologic findings of Domino, suggests that the so-called limbic system may be especially vulnerable to the effects of reserpine. It must be remembered that animal experimentation cannot completely answer this question because of the lack in animals of a well-developed symbolizing and integrating neocortex, which so greatly modifies subjective experience in humans and leads to so-called higher adaptive behavior. Herrick, according to MacLean,[11] reasoned that the rhinencephalon serves as a nonspecific activator for the cortex, fa-

cilitating or inhibiting learning, memory, overt behavior, and internal attitude. Only by work with humans can we learn about the effects of this drug on humans.

Interference between the anterior thalamic nuclei and their cortical representation in the cingulate gyri presumably would produce some of the psychiatric effects of the drug that have been likened to those of lobotomy.

Zeller and associates [12] commented as follows:

> Because of the rather specific action that these drugs have upon these areas of the brain, they seem to produce an effect similar to that seen in patients with lobotomy. Some have described this effect as a peculiar insulation of the patient against incoming stressful stimuli from the environment. From the psychodynamic standpoint, such an insulating effect is important. Stressful stimuli arising from within or from without the individual usually evoke anxiety, and each individual handles his anxieties according to previously learned ideational and behavioral responses. If the emotionally upset patient can be guarded against incoming stressful stimuli that potentially can further upset the homeostasis of his internal environment, he will be better able to mobilize his previously learned defenses and coping mechanisms in order to handle more efficiently the anxiety or affect evoked by the forces that threaten him from within and from without.

We agree entirely with their formulation of the insulating effect of the drug and agree that this insulating effect produces a tranquilized state in persons who have a poorly integrated ego structure and sensitivity to overwhelming environmental stimulation.

We shall present evidence to show that this tranquilized state is a threat to adaptive behavior in some persons and shall attempt to deduce how a physiologic event in the nervous system can produce profound psychodynamic effects that are interpreted by the patient as coming from his environment.

Shortly after reserpine began to be used as an antihypertensive drug, Freis [13] reported two cases in which agitated depression had developed while reserpine was being administered. Wilkins,[14] Dustan and coworkers,[15] Kass and Brown,[16] and others have mentioned other instances of depression but have provided little in the way of descriptive data or explanation of the syndrome.

One of us (R. W. P. A.) and associates [17] undertook a "double-blind" study of reserpine to test its antihypertensive effectiveness. In the course of this study, 10 of the 58 patients observed became sufficiently depressed and agitated to warrant discontinuance of the drug. We [18] have reported briefly on these and other similar cases and proposed a tentative explanation.

Present Study

Since reserpine began to be used clinically, we have seen 42 patients at the Mayo Clinic in whom administration of this drug had led to reactive depression. All these patients have been seen in psychiatric consultation; many more patients with milder depression have been cared for by our cardiovascular colleagues without psychiatric consultation.

These patients did not recover when administration of the drug was stopped. Instead, the depression continued and was indistinguishable from ordinary depressive reactions. Of these 42 patients, 12 had electroshock therapy and recovered uneventfully. The rest were not judged to be incapacitated enough for treatment or else refused it. Two patients committed suicide.

The role played by reserpine in this syndrome must be judged with care. Factors in the life situation frequently can be found to explain the depressive reaction that was concomitant with administration of reserpine.

> Case 1.—A 38-year-old man came to the Clinic complaining of feelings of agitation and depression, with a typical sleep pattern of a reactive depression. He had an excessive emotional investment in his hobby of flying. He had undertaken flight inspection of the high-tension power lines that his utility company maintained. Because of governmental requirements, it was necessary for him to obtain a commercial pilot's license. In the course of attempting to obtain such a license it was noted that he had hypertension that exceeded the limits required for issuance of such a license. Thereupon, he had been given reserpine, which decreased his blood pressure but not sufficiently to allow him to pass the examination. He had been forced to give up flying. His depression began

subsequent to this. It is obvious that many other factors were operative in his depression in addition to any possible effect that reserpine could have brought about.

In other patients, the discovery of hypertension or the prescription of medication for it, in spite of the fact that the physician previously had minimized the severity of the disease and had not treated it at all, may be enough to set the train of diminishing self-esteem in motion.

Case 2.—A 63-year-old man came to the Clinic suffering from the classic signs and symptoms of a reactive depression. He had received medical care over a long period, during which the severity of his illness continually had been minimized; he had been reassured that treatment was not necessary. Four months previously, during a routine check, comment had been made on the height of the patient's blood pressure and reserpine had been prescribed. Because his father had died after a cerebrovascular accident consequent to hypertension, the patient became quite alarmed about the status of his own health, and his depressive reaction began almost immediately.

The frequency of depression in older patients is great, and careful history taking is necessary in order to establish the fact that a depression had not been present before medication began. We have seen a number of patients who have been treated for agitated depression by means of reserpine and who have become much worse under this regimen. It is our impression that such patients are much more likely to have the parkinsonian side effects of reserpine than are originally undepressed patients.

The 42 patients in our study did not include any such as those in the foregoing case reports, but included only those who did not have clinical depression prior to medication and in whom careful psychiatric probing could elicit no data to indicate shifts in their interpersonal situation that could lead to a depressive reaction.

The 42 patients gave rather uniform accounts of the development of their difficulties. The first few doses of the drug frequently made them anxious and apprehensive. As medication was continued, they reported increasing feelings of strangeness, verbalized by statements such as "I don't feel like myself;" "Things don't seem right any more," and "I'm afraid of some of the unusual impulses that I have." Many found that the dreams and fantasies experienced under medication were disturbing to their become more introspective and attempted to psychic economy. These patients tended to explain the change in their perception of themselves by all sorts of rationalization with regard to the events occurring in their life situations to which they ordinarily would not attend. Spontaneous recovery occurred if administration of the drug was discontinued early in this stage, in which beginning feelings of depersonalization and isolation or strangeness were reported. If, however, the process continued so that the depressed affect became clinical, discontinuance of the drug did not abort the reaction and the depression lived out a life of its own that was indistinguishable from depressions not associated with use of reserpine. However, it was our impression that patients who gave histories of previous clinical depression were more likely to show this picture if Rauwolfia compounds were used in the management of hypertension.

Comment

Saul [19] emphasized the repressed or suppressed rage that is close to the surface in persons who have essential hypertension. It has been postulated that such persons have chronic, unexpressed rage because of an inability to satisfy either their "oral" demands or their ambitious independent strivings. We were impressed by the number of treated depressed patients with hypertension who fit this description. Their need for narcissistic supplies usually outweighs their independent strivings, and they tend to placate the significant figures in their environment, fearfully watching for cues in order to ward off behavior they fear would lead to rejection. Any interference with perception of the environment is interpreted as a threat by these people, and many refuse to succumb to the "tranquilizing" effect. These persons are prone to depression and need constant replenishment of their narcissistic

supplies; any threat to this replenishment causes an ego collapse into a classic depressive position.

As already indicated, we agree entirely with the stand taken by Zeller's group,[12] especially with regard to their inclusion of stressful stimuli coming from within as causes of anxiety. It is our hypothesis that the interruption of impulses from subcortical centers to certain cortical regions may be interpreted as a cutoff from narcissistic supplies or a change in internal attitude by the symbolizing, aware, integrating cortex.

It appears to us that present neuroanatomic, neurophysiologic, neuropharmacologic, electroencephalographic, and anthropologic data indicate that reserpine exerts its influence by phenomena of neurochemical competition in or around the diffuse thalamic projection system and the paleocortex. Since reserpine apparently has little effect on the cortex itself, the patient seeks the cause of his altered state in his external environment and reacts as if his source of oral dependent gratification is lost, such reaction occurring in the form of depression.

Rado[20] has touched on this phenomenon. He says:

> Freud used "latent," "hidden," and other cognate adjectives as equivalent to "unconscious." We suggest *non-reporting* be added to this list. Terms qualified by any one of these adjectives are extrapolated psychologic terms. Speaking, for instance, of an *unconscious* or *non-reporting desire*, the investigator refers to a missing causal agent, which . . . acted as if it had been a *desire*, though in fact it was a purely physiologic event. Since the psychologic meaning of non-reporting nervous activity can be arrived at only by this process of psychologic inference, naturally it can be expressed only in an extrapolated language of psychology.

It is, of course, necessary for patients to use this extrapolated language of psychology in telling us what they feel and also to interpret it in relationship to external environment.

MacLean[11] spoke of the same phenomena in neurophysiologic terms. He quoted Papez' theory that "the hypothalamus, the anterior thalamic nuclei, the gyrus cinguli, the hippocampus and their connections constitute a harmonious mechanism which may elaborate the functions of central emotion, as well as participate in emotional expression." MacLean cited evidence that the orbitomesial surface of the frontal lobes, the anterior insula, the temporal pole and the pyriform-amygdaloid complex should be added to this system and referred to as the "visceral brain."

This "old brain" in primitive form is the highest correlation center for ordering affective behavior of the animal in such basic drives as obtaining and assimilating food, fleeing from or orally disposing of an enemy, and reproducing. Evidence is at hand that it subserves the same function in man. MacLean[11] stated:

> Considered in the light of Freudian psychology, the visceral brain would have many of the attributes of the unconscious id . . . but rather eludes and primitive structure makes it impossible to the grasp of the intellect because its animalistic communicate in verbal terms.

In Rado's terms, its activity is nonreporting. Our patients' terms were "I do not feel like myself," and "I feel so strange."

It does not appear likely that any drug can cause the complex psychologic events necessary to precipitate a psychiatric illness by pharmacologic means alone. It is likely that psychologic language by both the patient and the physician and the physiologic event of diminishing or interfering with primitive emotional forces for survival reaching the symbolizing, verbalizing, and integrating cortex result in reorganization of cortical activity. This reorganization interprets the change as coming from outside and reacts accordingly. It appears possible that removal of the physiologic interference after the psychologic misinterpretation has taken place often is not sufficient to allow the organism to return immediately to its former mode of functioning; perhaps this cannot be attained at all without treatment.

On the other hand, reserpine has its most dramatic usefulness in those situations in which the primitive animalistic demands overwhelm, or threaten to overwhelm, the symbolizing, verbalizing, integrating, corti-

cally mediated adaptive pattern. It is in the panicky maniacal person that dampening of primitive demands without narcotization of cognitive functions will allow remarshaling of forces and, with psychologic support and therapy, will allow the cortex to resume its mediating function between adaptive social behavior and the demands of the primitive emotive system.

Summary and Conclusions

A series of 42 patients who had reactive depression associated with the use of reserpine has been observed at the Mayo Clinic. Most of the patients had essential hypertension.

To explain these events, it is assumed that reserpine acts in diminishing the impulses from subcortical thalamic centers to the paleocortex or hippocampus. It is assumed also that the symbolizing cortex interprets the change in its dynamic position as being due to a change in the external instead of the internal environment.

The literature most pertinent in the elucidation of the mode and site of action of reserpine is reviewed briefly.

The Mayo Clinic.

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A Definition and Analysis of Depression

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In this paper we define depression and postulate three forms of its pathology. The definition leans heavily upon the understanding of hope, which Lewin [4] and French [3] have suggested. It also derives from and leads back to laboratory experiments concerned with small-group behavior. In effect, this paper asserts a conceptual model of depressions whose primary purpose is to make feasible the experimental production of depression, its equivalents or its various components.

The current analysis began when my colleagues and I observed some unintended results of an experiment concerned with the initiation of cooperation.[6] Two events appeared which seemed as important as the intended outcome. First, although we openly explained the experiment to all subjects, both during and after the trials, a large number of those who failed the task later reported that they had experienced intense depression subsequent to their failure, which remained for several days. Second, although the task clearly required the rational use of complete information, many of the subjects seemed to rely upon their preferred action patterns. They resisted the influence of the information.

An analysis of that task reveals three kinds of factors underlying the subject's subjective probability of goal attainment: (1) chance factors in the physical arrangement of the pertinent instruments in the world; (2) three circumscribed action patterns, among which the subject was forced to choose, and (3) the concordance of an action pattern, the time available, and the collaborators available. We were led to contend that the hopefulness generated by these three factors is of primary significance in pathological depression.

Stimulated by this general analysis, as well as by other interests, we began to examine the work habits of depressed persons in our occupational therapy program. Among other things, we noted a preference for repetitive tasks, jobs in which the same motions succeed one another with monotonous regularity. When one object was completed, these people sought work requiring identical actions. They seemed to limit themselves to single-action patterns, using the repetitive task in much the same way that compulsive persons use rituals. They were reluctant to initiate tasks; and, when pushed into action, they demanded excessive help and attention. They appeared to be checking the constancy of the occupational therapy worker and divesting themselves of any responsibility for failure. Furthermore, they usually began large projects which they expected to achieve rapidly and were visibly disappointed when they realized they could not fulfill their ambitions. These observations, together with the analysis of the experimental task, encouraged me to construct a model of depression appropriate, it is hoped, for research along the lines of current thinking in small-group behavior analyses.

Core of Depression

We propose that depression be seen as a manifestation of felt hopelessness regarding the attainment of goals when responsibility for the hopelessness is attributed to one's personal defects. This definition of depres-

Received for publication Nov. 15, 1956.

Institute for Psychosomatic and Psychiatric Research and Training, Michael Reese Hospital.

This study was conducted as part of a program of research on depression under the Michael Reese Foundation's Fund for Psychiatric Research Grant 54-126.

sion emphasizes (1) the feeling of hopelessness, (2) the feeling of responsibility for the hopelessness, and (3) the context of goal-directed behavior accompanying the feeling of hopelessness.

In its present usage, hope corresponds to the conception (not necessarily conscious) that some time in the future one's desires and the real situation will be mutually compatible and rewarding; that is, with some degree of assurance, one expects to be able to reach currently desirable goals. Thus, the hope of reaching a goal is a function of the perceived probability of success (i. e., expectancy of success) with respect to goal attainment. The feeling of hope reflects an estimate of high expectancy, and the feeling of hopelessness a very low expectancy, of success.

We do not imply that hopelessness is identical with depression. Both mourning reactions and apathy manifest hopelessness without fitting the definition, for they do not derive primarily from a felt responsibility for that hopelessness. Similarly, panic reflects hopelessness but not the assumption of responsibility. While hopelessness is necessary for depression, in the present view, it is clearly not sufficient.

Three Orientations of Expectancy

In this section we describe and relate to one another the expectancies derived from the factors in the experimental task noted above. We shall later refer these expectancies to aspects of ontogenetic development.

The first orientation is an *expectancy associated with a generalized goal*. It refers to the perceived probability that any felt need will be satisfied. The success in this case would be determined without reference to the person's own behavior. It answers the question: "If I merely exist, what are the chances that any need I may have will be satisfied?" It reflects the proportion of all the person's needs that have been satisfied and the completeness of that gratification.

The second orientation is an *expectancy associated with a behavior style*. It refers to the perceived probability that a particular style of behavior will increase one's chances of reaching any goal that may appear. The enhancement of chances for success on a generalized goal is seen to depend primarily on the preferred way of relating to others. "My chances of success are better if I am dominant or deferent or passive or masculine or affiliative, no matter what the goal is." This is the "personality trait," for example. In a sense, it is the person independently of the immediate situation; just as the first orientation of expectancy concerns the environment independently of the person.

The third orientation is an *expectancy associated with the particular situation*. It is dependent upon the analysis of different actions under varying circumstances which result in different situational probabilities of success. (Consciousness is not necessarily to be inferred from "analysis".) Preferred actions are modifiable to accord more with the particular goals and instruments. And the goals are modifiable toward greater unity with one's preferred style of life. Unlike the first two expectancies, this depends upon information about the confronting reality.

The three orientations may be seen as levels of differentiation of the subjective probability of success (i. e., expectancy) concerning any momentary need. The expectancy associated with a generalized goal is the least differentiated orientation, and that associated with the particular situation, the most differentiated. We propose that three forms of depression can be distinguished according to whether the hopelessness is connected with one or the other of these three orientations of expectancy, and, further, that if hopelessness is associated with a less differentiated level of expectancy, hopelessness for the more differentiated levels is implied, although the reverse is not true.

Three Forms of Depression

In this section we trace the implications of the hopelessness in the three forms by considering the following aspects: 1. To what class of events is the hopelessness attached? 2. In what way is the person responsible for the hopelessness? 3. How do the hopelessness and felt responsibility distort the person's time perspective? 4. How do the hopelessness and felt responsibility distort the person's interpersonal relations? 5. How do the hopelessness and felt responsibility distort the person's perceptions of the availability of collaborators? 6. How does the hopelessness distort the person's perceptions of secondary gains and losses? The description of the forms of depression emerges from a conceptual analysis of the ramifications of the orientations of expectancy in these six areas.

Tables 1 and 2 present a schematic summary of the discussion below. In the development of the three forms we proceed from the mildest to the severest form. Starting with a reasonably healthy adult, the most differentiated expectancy, that associated with the particular situation, is likely to be first disturbed.

Form I Depression.—This form manifests a felt personal responsibility for hopelessness connected to the expectancy involving the particular situation. By the application of the felt responsibility to the characteristics of this orientation of expectancy, we derive the phenomena which should appear with this sort of depression.

1. The hopelessness involves a specific goal and a specific set of persons or things vital to the attainment of that goal. At this stage of depression the person is concerned with the manipulation both of the immediate goal and of the relationships aimed at goal attainment. The self-abasement is not highly generalized, and, indeed, if pressed, the person can readily admit his competence and ability in other areas of life.

2. The felt inadequacy revolves about the inability to establish congruence between goal demands and the wishes of potential collaborators. The person can foresee a decent possibility of goal attainment or of establishing good working relations. But the two requisites do not mesh. If other persons or things were available, his skills might be adequate to the task; if other tasks were available, these persons or things would be perfectly suitable. But his skills are not sufficient to overcome the discrepancy between these classes of demands. If he had more capability, the weaknesses of his collaborators or the excessive demands of the task could be met. It is his "fault" that goal attainment is improbable.

3. The person believes that with his skills the goal cannot be reached in the time available. Either the time needed to reach the goal may be overestimated or the time available may be underestimated. The time needed is a function of the complexity of the task and the skills and instruments which are accessible. The complexity will be exaggerated and the skills depreciated. The time available is determined more independently. One must reach a goal before the storm comes, before the semester ends, before present supplies run out, before other demands take one's partners away, before the goal fades. In each setting the person will tend to see the time available as shorter than it actually is. This error, like other manifestations of this form of depression, has relevance primarily to the goal under

TABLE 1.—*Success-Probability Ranges in Three Depression Forms*

Orientation of Expectancy	Depression Forms		
	Form I	Form II	Form III
Particular situation	High→zero Middle	Zero	Zero
Behavior style	High→middle	Middle→zero	Zero
Generalized goal	High	High→middle	Middle→zero

consideration. There is little generalization to other goals until the person is changing from this form of depression to a severer one.

4. With respect to interpersonal relations, the person feels that his preferred styles of behavior interfere either with the establishment of good working relations or with the goal to be reached. With the particular goal, his likely behavior will alienate his friends or co-workers. With the specific friends, his attempts at harmonious activity will hinder goal attainment. He thus conceives himself as an undesirable person, although, again, when he implies that he is not lovable, he means to limit this to the current context. He can be prodded into admitting his desirability in other circumstances.

5. He is also likely to assume that others actually have the proper capacities but, because he is primarily responsible for the hopelessness of the attempt, they will not offer their talents to him. It would seem to follow that he would tend to overestimate the skills of others. An error in this direction would maintain the consistency of own responsibility as contrasted with other or joint obstacles to success. The capacities of others will be seen interdependently with his own—the less he possesses, the more they have, and the less willing are they to carry him along.

6. Finally, this sort of person will overestimate secondary losses and underestimate secondary gains to be gotten from the activity. For example, because he is weak on the necessary skills, he must depend more heavily upon others; but others demand more for the added burden. The more this is true, the more likely is he to incur secondary losses and the less likely is he to get secondary gains. (The losses and gains are reciprocals, since they both deal with all other needs than those which the task is designed to fulfill.)

As expectancy of success associated with the particular situation approaches zero, the other expectancies decrease in hope and the person relies increasingly upon an expectancy associated with a behavior style. The less differentiated expectancy is seen interdependently with the more differentiated one and thus decreases in hope with it, although it decreases at a slower pace.

Form II Depression.—This form manifests a felt personal responsibility for hopelessness concerning an expectancy associated with a behavior style. The person with this form assumes that the most differentiated expectancy leads to no hope at all.

TABLE 2.—*Summary of Three Depression Forms*

Distinguishing Factors	Forms of Depression		
	Form I	Form II	Form III
1. Class of events to which hopelessness is attached	Congruence in a goal, a behavior style, and specific collaborators	Preferred styles of behavior on a generalized goal	General provision of satisfaction by the environment
2. Manner in which the person feels responsible for the hopelessness	Own goal inappropriate to collaborators, and they have inappropriate goals	Cannot establish relationship styles that bring eventual satisfaction	Person is worthless in all ways
3. Distortions of time perspective	Time needed to reach goal too great and time available too short	Time needed on any task reflects time needed on most difficult task; time available reflects minimum time available for most difficult task	Immediate gratification or none at all; specious present equivalent to eternity
4. Distortions in interpersonal relations	To reach goal social relations with specific others impaired; good social relations impede goal attainment	Behavior style in which person has maximum power when in action, minimum power when not in action	Active passivity; ward off induction of activity
5. Distortions of perceptions of availability of collaborators	Co-workers have superior skills, and they underestimate depressive's skills; they are unlikely to collaborate	Distrust that others will withdraw support upon discovery of depressive's weakness	Cannot conceive that others will work with him; possible delusions that others wish him to act so they may torment him
6. Distortions in potential secondary gains and losses	Secondary losses overestimated and secondary gains underestimated	No distinction between primary and secondary gains and losses; all of equal value	No distinction between primary and secondary gains and losses; all of equal value

1. Hope and despair revolve around the style of behavior to be expressed, so that the person is not activated by the appearance of a goal. He will seldom initiate goal-directed actions. He is already aware that in any particular case he is bound to cause failure for himself as well as others. (His expectancy associated with the particular situation is zero, and it is this set which is directed to immediate goals.) He acts on the world from one of two impelling forces: (1) Others induce him into action by urging his favored style of action, or (2) he aims to reestablish a behavior style with adequate chances of success.

2. The felt inadequacy refers to the perceived unlikelihood of being able to establish relationships toward a generalized goal which will lead to goal attainment. The major skill lack here has reference to all goals, not to the immediate one. Generalized abasement appears. The person feels hopeless because he can never bring about success—he does not yet feel unworthy of being given to. If he does achieve success, the cause is located in others.

3. When the person is put into action on a task, he displays characteristic behaviors, which become more pronounced as this orientation of expectancy tends to zero. Because he is striving as if he were going toward a generalized goal, he treats each task as a representative of all tasks, overlooking the idiosyncrasies which any special task may have. But, additionally, since a low probability of success by means of a behavior style has been induced through failure of the higher level of expectancy, he considers each task as the most difficult of all tasks. Therefore, his behaviors are geared to maximum effort and efficiency when he is provoked into effort.

If the time available for reaching a goal is assumed to be inadequate, and still the person is struggling toward the goal, then, somehow, the time perspective must be proved wrong. Actions must be geared to defeating time. Either the time available must be prolonged or the time needed shortened. Since time would have to be consumed in attempts to prolong time available, efforts in this direction will be restricted to long-term goals. More commonly, we suspect, the person will entertain actions which alleviate time needed. The most obvious means of accomplishing this aim consists in speeding up one's actions. If the person works faster than he presumed he could, he will be able to demonstrate an error in his time perspective and he will be able to reach the goal. A second way to contradict a time perspective is to work flawlessly. By being completely accurate, the person will maximize the chances of a successful time period. That is to say, he will approach the minimum time needed. Concomitantly, he will tend to demand accuracy on the part of others and will feel hopeless when some errors appear.

4. With a low chance of success, the behavior style which is required is that in which the person has maximum power. The argument for this inference follows from the one above about maximum effort on the task. The person treats the special relationships as but representative of all relationships and as the most difficult of all possible ones. Thus, he strives for maximum domination of other persons and things. But this domination is not geared to the unique characteristics of the persons and things around, so that it is not embodied in behaviors which might get maximum results in the particular situation. Being oriented toward a generalized goal, the form of the dominance attempt consists of "pure" power striving: a temper tantrum or rage. When he is provoked into action, therefore, the person becomes enraged with the inducing person *and* with others in the field. He is angry not because he has been forced to act, but because this is the only action he can see as possibly leading to success.

5. Suspecting that others will withhold their skills the moment his power over them fails, the person is led constantly to check upon whether his collaborators are still with him and will remain until the end. He fears

sudden withdrawal of support, since the other persons may discover that his power is unreal. He will very likely introduce a system of checking, which, again, is inappropriate to the task because he is striving toward a generalized goal. (We may note how closely allied to paranoid behavior this may appear. The suspicion is based on the necessity for the person to control others by means other than his skills. When the deceit becomes primary, we would expect delusions; but when the collected determinants are relatively equal, we would look for distrust of the constancy and responsibility of the collaborators.)

6. Since he is dealing with a generalized goal, he does not distinguish between primary and secondary gains and losses. Every gain or loss is primary, and every gain or loss affects the hopefulness in an expectancy associated with a behavior style. Thus, any incidental setback is confirmation of his hopelessness, so that his rage, suspicion, concern with order, and efficiency may seem doubly inappropriate.

As the hope in this expectancy approaches zero, the person relies increasingly upon an expectancy associated with a generalized goal and he gradually becomes a Form-III depressive.

Form III Depression.—The patient manifests a felt personal responsibility for hopelessness concerning an expectancy associated with a generalized goal. As expectancy of success associated with a behavior style approaches zero, the hope associated with a generalized goal also decreases. The person relies, however, on this last hope.

1. The hopelessness of this depression contains the belief that satisfaction is never possible. Neither behaviors by himself nor action of others, and especially the latter, can lead to gratification. This assertion follows from the statement that this orientation of expectancy has reference to externally created successes and failures.

2. General unworthiness is the standing feeling. On the one hand, the person is responsible for the lack of success; on the other hand, the world does not provide it; together, these mean that the person is not valuable enough to be given satisfaction. And this refers to generalized goals, so that the person conceives himself as totally worthless.

3. Because he assumes that his own efforts are useless, he believes that tasks have immediate gratification or none at all. Neither time nor space can intervene between the arousal of a need and its satisfaction, for these would entail failure. His time perspective is grossly disturbed. Because he is so extensively inadequate, he believes that only excessive time available would permit goal attainment. The specious present alone becomes meaningful, with any future equivalent to the longest future, to eternity.

4. Even others will not now move him into action. First, he surrendered his own initiative from depreciation of it. Then he relied on his control over others. But all striving is futile, so that he must deny any effort toward achievement. However, he recognizes that others are goal-directed. Therefore, he must strive to maintain passivity—he must prevent himself from being active in any task-oriented situation. He must have no interpersonal relations.

5. He may, in his efforts to be passive, have delusions that others are trying to make him struggle, only to pull away from him and torment him with his failures. Otherwise, no one would be willing even to be with him, no less work with him.

6. There is no distinction between primary and secondary gain and any distinctions between great losses and grave losses fade.

The Three Orientations of Expectancy Viewed Developmentally

The three orientations of expectancy represent successive differentiations of goal direction in the growing child. As products of developmental periods they parallel most closely Ferenczi's [2] "stages of development of a sense of reality."

The expectancy associated with a generalized goal is a result of the infant's helpless

position. The infant must assume that with the emergence of a need will come immediate satisfaction. In two connections the events that actually occur induce an expectancy on a generalized goal: (1) A probability is associated with relative frequency of success in the long run, and (2) a probability is involved in the activities necessary to the gratification of each particular need. On the one hand, a residue is left with the child according to the proportion of successive needs which are satisfied. On the other hand, a residue is formed according to the extent to which the child's entire matrix of needs is gratified in the attainment of each single goal. This stage is Ferenczi's "period of unconditional omnipotence." Erikson [1] refers to this stage as the foundation period of "basic trust."

The second stage (creating an expectancy associated with a behavior style) is marked by the child's recognition that his actions are partly responsible for his success or failure. He perceives that his behavior puts him into certain relationships with others and that this influences the outcome. He aims to raise the probability of success on a generalized goal by creating that kind of relationship most tied with success. The expectancy is determined by two source classes: (1) the current experienced successes of specific behavior styles, and (2) the past successes embodied in the expectancy on a generalized goal. When the 2-year-old asserts his independence, he is playing with styles of behavior. He has rituals; he imitates; he tries the same activity on many different persons and things. The styles he is prone to experiment with are not randomly selected, however; they are the styles most congruent with his summary of the world's kindness, his basic trust, his hope on a generalized goal. This stage is covered in Ferenczi's three intermediary periods from magical hallucinatory behavior through speech. Piaget [7] speaks of the development of the "idea of participation" and of "magic" in discussing the child's ideas about the world in this period.

The expectancy associated with the particular situation comes when the child learns that his strivings must be oriented toward a congruence between the relationships to be established and the goal to be achieved. As Ferenczi says [8]:

> The feeling of omnipotence gives way to the full appreciation of the force of circumstances. The sense of reality attains its zenith in Science, while the illusion of omnipotence here experiences its greatest humiliation: the previous omnipotence here dissolves into mere "conditions" (conditionalism, determinism).

The child is guided by the reality principle, recognizing his own determining influences and those of others around him.

Comment

We believe that the three forms of depression presented above detail the factors underlying the conventional diagnostic distinctions in this area of psychopathology. Form I is presumed to be the conceptual model of neurotic depression; Form II, of agitated depression, and Form III, of retarded depression. Confirmation of this conceptualization obviously must await clinical and experimental research.

Pending such confirmation, the model lends itself to the planning of experiments involving the production of depressions or their equivalents. The feasibility of applying the model in this manner is suggested by its relevance to existing experimental knowledge. *Form I depression*, being closest to healthy functioning, seems more available for research than others. The level-of-aspiration studies, summarized by Lewin,[6] seem to meet some of the central requirements of the model. He notes [9]: "We speak of *aspiration* in regard to an action if the result of this action is seen as an achievement reflecting one's own ability." Thus, in level-of-aspiration studies one component is the assumption by the subject of responsibility for success or failure. Furthermore, the subject is involved in setting the goal according to his ability and performance, thus modifying both goal and his own behavior. Although time is not usually manip-

ulated in such studies, there seems to be no reason that it cannot be controlled. Nor do level-of-aspiration studies seem to preclude collective behavior, which can be handled to account for the interpersonal requirements in the model, as well as for the secondary gains and losses. These kinds of tasks seem especially pertinent in that we know many of the devices that people use to avoid the feeling of failure and to ward off depression. Controlling these permits the depressive reaction. Lewin mentions, for example[10]: "If a lowering of the level of aspiration is made impossible, the maturity of aspiration may regress . . .; that is, a procedure is used which is characteristic of a younger age level." The findings concerning techniques for avoiding failure prepare us to eliminate the healthy counteractive measures which maintain the subject's emotional equilibrium. Armed with knowledge of aspiration, not only in adults, but in developing children of many ages, we stand an excellent chance of bringing psychopathology into the experimental laboratory.

The usual small-group experiment is less appropriate for the induction of the severer depressions. In any single instance it is difficult to create perceptions and behavior directed toward a generalized goal. More likely than not, the subject will attack the real, immediate goal and divorce it from the remainder of his life and the world. It may be that with limited understanding of the ways in which to induce actions toward a generalized goal, we shall be forced to work with people whose personalities are already operating on that level or are very near to it. For instance, it might be necessary to evoke agitated depressions by having as subjects persons who are already neurotically depressed. These people would help to by-pass the two stages of experimentation necessary if one were to take healthy persons through a neurotic depression into an agitated one.

This model of depression seems to suggest other types of research also. The social emotions, such as hope, faith, optimism, and trust, are constantly raised as important topics by personality theorists and clinicians. Casual inspection hints that faith and trust, for instance, seem to vary along the dimensions of the orientations of expectancy outlined in the text. There is religious faith, blind to any cognitive struggles; and there is the faith of the scientist in his understanding of events. Similarly, there is an underlying, general "basic trust," and there is trust derived solely from one's control over immediate events. These faiths and trusts seem to follow the various hopes that we have postulated, being based on the different orientations of expectancy and bearing implications about the other orientations. We should expect, for instance, that reliance upon a "basic trust" would be one thing when coming from uncertainty about one's ability to evaluate the immediate situation properly. It would be another thing when serving in a new or strange situation to permit the situation to make itself known. In the first case we would see distrust, as we see hopelessness in the Form III-depressive. The more differentiated grounds for trusting are rejected because they do not help, and they affect the level of trust in the more primitive orientation. In the second case we would find acceptance until conditions warrant otherwise. The model would seem to make these social emotions more available for research.

Summary

Depression is defined as a manifestation of felt hopelessness regarding the attainment of goals when responsibility for the hopelessness is attributed to one's personal defects. In this context hope is conceived to be a function of the perceived probability of success with respect to goal attainment. Three orientations of expectancy are described: (1) an expectancy associated with a generalized goal; (2) an expectancy associated with a behavior style, and (3) an expectancy associated with the particular situation. The three orientations are traced on the following questions: 1. To what class

of events is hopelessness attached? 2. In what way is the person responsible for the hopelessness? 3. How do the hopelessness and felt responsibility distort the person's time perspective? 4. How do the hopelessness and felt responsibility distort the person's interpersonal relations? 5. How do the hopelessness and felt responsibility distort the person's perceptions of the availability of collaborators? 6. How does the hopelessness distort the person's perceptions of secondary gains and losses? The three orientations of expectancy are viewed developmentally. Finally, the research implications of the model are suggested.

Drs. Harold Basowitz, Jacques Chevalier, and Roy R. Grinker read the manuscript and made many helpful suggestions. Cynthia Board, Jane King, and Anna M. Tierney participated in a seminar with the author, in which the work habits of depressed persons were examined. Their efforts were very helpful in the formulation of this model.

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The Convulsive Threshold in Schizophrenia

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Interest in the convulsive threshold of schizophrenics was aroused by Gastaut in 1950, when he postulated a "thalamic factor" in schizophrenia after finding a lowered "myoclonic threshold" in persons with known diencephalic organic lesions and in 70% of schizophrenics.[1] These findings were supported by observations of Bickford and Daly[2] but not by those of Kershman.[3] Complications and ambiguity in the method of measurement were reported.[4,5] With controls for these factors, a new study was begun by Leiberman and Hoenig, and by 1953 it seemed that only catatonics had a low threshold and that the threshold varied with the clinical state of the patient.[6,7] The low threshold was interpreted as "a tendency of a presumed diencephalic neuronal system to discharge more readily than in normal individuals."[6] Chamberlain reported no change in threshold during remission of the illness and felt that the threshold was determined by constitutional factors, since a leptosomatic habitus was correlated with low threshold.[8] Leffman and Perlo restudied the problem and reported in 1955 that 53% of schizophrenic patients had a low myoclonic threshold, as compared with 2% in psychoneurosis and character disorder. They concluded that the "finding of low myoclonic thresholds in schizophrenic patients is of great interest, since it indicates an alteration from the normal in a subcortical mechanism in these patients." They found that "electroshock had an immediate effect of raising the threshold," but that this "was of temporary duration" and that "the patient with a basic schizophrenic personality continues to have a low myoclonic threshold."[9] Several authors claimed that a low threshold predicted successful outcome in therapy.[10-13]

A definitive evaluation of the convulsive threshold in schizophrenia awaited the development of a reliable and valid method of measurement. Such a method needed a clearly defined end-point, which is reached without having a seizure, but which must have a high correlation with the point at which a seizure will actually occur. Photometrazol activation has been widely used for this but has not seemed ideal.[14,15] Although it had been reported that generalized convulsive seizures raised the threshold to subsequent seizures,[14-16] studies of threshold in schizophrenia did not always control the factor of concomitant convulsive therapy and of inadvertent seizures obtained during the measurement of threshold. The present study attempts to eliminate these variables.

Method

Convulsive thresholds were obtained on 30 patients with schizophrenic reaction and on 20 nonschizophrenic patients with other psychiatric diagnoses (Table 1). From consecutive admissions to a 200-bed, acute psychiatric service all those meeting the following criteria were selected: age 16-40 years; no personal or family history of epilepsy; no vague "spells" or repeated syncopal attacks; no history of head injury with unconsciousness; no abnormal cerebral dysrhythmia or

Received for publication Dec. 5, 1956.

Miss Margaret Johnson, B.S., R.N., gave technical assistance.

Hexazole (4-cyclohexyl-3-ethyl-1:2:4-triazole) was supplied by Mallinckrodt Chemical Works, of St. Louis, under the trade name Fazole.

Department of Psychiatry and Neurology, Washington University School of Medicine, and the Research Laboratories of Malcolm A. Bliss Psychopathic Institute.

This study was supported in part by a research grant from the National Institute of Mental Health of the National Institutes of Health, U. S. Public Health Service, and by funds from the Neuromedical Foundation of St. Louis.

TABLE 1.—*Description of Schizophrenic-Nonschizophrenic Groups*

	N	Mean Age, Yr.	Sex		Mean I.Q.*	Duration of Illness	
Schizophrenia			Male	Female		Less Than Six Mo. (Acute)	More Than One Year (Chronic)
Total	30	28.6	18	12	99.6	12	18
Paranoid	8	32.5	2	6	106.4	3	5
Catatonic	4	28.5	4	0	113.0	2	2
Undifferentiated	18	26.9	12	6	93.7	7	11
Nonschizophrenia							
Total	20	25.6	13	7	108.9	--	--
Psychoneurotic disorder	4	27.0	1	3	110.0	--	--
Sociopathic personality disorder	7	23.4	6	1	107.1	--	--
Personality trait disturbance	7	25.1	5	2	106.3	--	--
Psychotic depressive reaction	2	31.5	1	1	121.5	--	--

* Based on four verbal subtests of Wechsler Bellevue Scale for Adults.

electroencephalogram; no organic disease; no mental deficiency or language difficulty; no lobotomy; no convulsive therapy for three months; no anticonvulsant or ataractic drug within two weeks; no sedative or other medication for 24 hours; patient not pregnant, not menstruating, and on regular hospital diet with no breakfast on morning of threshold measurement; routine blood count and urinalysis normal; serology negative, and sulfobromophthalein (Bromsulphalein), cephalin-flocculation, and thymol turbidity tests within normal limits. Diagnosis was agreed upon by three psychiatrists and one psychologist according to the official American Psychiatric Association nomenclature[21] (1952) after each had interviewed the patient.* Borderline cases were not accepted. Patients with schizoaffective reactions, schizoid psychopaths, and pseudoneurotic schizophrenics were excluded. The classification of acute schizophrenia was limited to those ill less than six months, and the term chronic schizophrenia was applied to those ill longer than one year; however, all were having a marked exacerbation of symptoms at the time of admission.

The measurement of convulsive threshold was by a photopharmacologic activation technique standardized and validated in our laboratory.[17] In a 10-second period 0.5 ml. of 1% hexazole was injected into the antecubital vein. Ten seconds was allowed for circulation of the drug to the cerebrum, and a flashing light was delivered with the eyes closed for 10 seconds. An electronic crater-lamp stimulator in a goggle arrangement (to exclude ambient light) was used at a frequency of 15 flashes per second.† The cycle of drug-time-light was repeated until generalized myoclonus was seen clinically and spike-and-wave or rhythmic polyspikes appeared in the E.E.G. Progression to a grand mal seizure was blocked by 150 mg. of secobarbital (Seconal) sodium available immediately through a three-way stopcock. The number of injections required to reach the end-point was taken as a numerical indicator of the convulsive threshold.

Results

The mean convulsive threshold for the schizophrenic and the nonschizophrenic groups is presented in Table 2. The threshold for the subtypes of schizophrenia is also listed in Table 2. No such breakdown was made for the nonschizophrenic group because of the small number of patients in

* Dr. Eli Robins and Dr. Lawrence N. McCullough collaborated in the diagnosis of patients.

† Manufactured by the Instrument Engineering Laboratories Company, Inc., St. Louis, Mo.

TABLE 2.—*Mean Convulsive Threshold for Schizophrenic and Nonschizophrenic Groups**

Schizophrenic	N	Mean Threshold (No. of Injections)	Standard Deviation
Total	30	6.5	3.07
Paranoid	8	5.3	3.17
Catatonic	4	6.5	2.40
Undifferentiated	18	7.0	3.13
Nonschizophrenic			
Total	20	6.7	3.10

Schizophrenic *vs.* nonschizophrenic $t=0.22$.

* All statistics based on small-sample technique.

each category and the heterogeneity of symptoms.

The results clearly indicate that no difference exists between the two groups. Of interest also is the highly similar variability about the mean in the two groups. In most physiological and psychological studies schizophrenics tend to show a greater variability than the "normals" or controls. The convulsive threshold does not seem to follow this pattern. No significant differences were found among the subtypes of schizophrenia, but the number of patients was small and a conclusive statement cannot be made. There was no difference between the thresholds of the 12 acute and the 18 chronic schizophrenics; the mean threshold for the acute group was 6.3 and for the chronic 6.7.

As the threshold has been reported to vary with the clinical state of the patient, six-month follow-up measurements were taken, along with an evaluation of clinical improvement, and compared with initial findings. Fifteen of the thirty schizophrenics were available at six months. Failure to return was due to refusal on the part of patients or to inability to return because of residence out of state, in another hospital, or in jail. Patients who did not return were both in and out of hospitals and did not constitute a biased group as to clinical improvement.

There was no significant difference between the initial threshold and the threshold six months later on the same patient. The mean threshold of the 15 patients who returned was 7.2. When the type of change was evaluated, six patients had a higher threshold, three patients had a lower threshold, and six patients showed no change. The mean change was 0.2 injection, which is not significantly different from zero or no change.

None of the 15 schizophrenics who returned at six months could be described as nonschizophrenic or completely cured, but 11 were out of the hospital functioning at some level in the community. When the threshold of these patients was compared with those still requiring hospitalization, no significance was found. The number compared is small and the period of evaluation relatively short, but the results suggest that the threshold does not vary with clinical state.

A correction for weight in establishing threshold has been emphasized by some[18] and said to be unimportant by others.[17,19] Moore et al. and Ulett et al. believed that their method of injection made a correction for weight unnecessary. The findings in this study reveal a relationship between weight and number of injections necessary to arrive at the threshold end-point. On the total sample of 50 subjects, the correlation was 0.64, a value which is highly significant and indicates that 41% of the variance is due to weight alone. This does not negate our finding of no difference between schizophrenics and nonschizophrenics, since the mean weights of the two groups were 135 and 139 lb. (61.2 and 63 kg.), respectively. However, a correction for weight would be necessary in a type of study in which one attempts to measure an absolute threshold value, for example, as an aid in the diagnosis of epilepsy.

Because of the limited age range of 16 through 40, no complete statement can be made concerning the relationship of age to threshold. Within this age group, based on the total sample of 50 patients, no relationship is apparent. The Pearson correlation coefficient is 0.07.

No significant sex difference is noted, $t=1.35$. The mean threshold for men is 7.1 (S. D. 2.77) and for women 5.8 (S. D. 3.40). The slightly higher mean for men is accounted for by the correlation between weight and threshold.

Comment

In undertaking this study, it was our hope that substantial support would be given to those scattered reports in the literature that imply a difference between the thresholds of schizophrenics and nonschizophrenics. Had

this been true, it would have encouraged others to join the workers who believe that the central nervous system of schizophrenics differs in some important neurophysiological or biochemical manner from that of patients with other psychiatric disorders. Although several authors from their studies of convulsive threshold have implicated the diencephalon as a possible seat of the basic disturbance in schizophrenia, our own investigation of convulsive threshold does not support this thesis.

We believe our results differ from some others in the literature because of differences in the technique of measuring convulsive threshold and in criteria for selection of the patient sample. We wish to underscore the importance of the latter in psychiatric investigations. Even though there may be regional and theoretical differences of opinion as to what constitutes a schizophrenic, we found that adherence to the American Psychiatric Association nomenclature was a good working rule. Our insistence, not upon chart diagnosis, but upon an agreement by three separate qualified and experienced psychiatrists from a judgment made by actual interview behavior by the patient, made us realize how many "schizophrenics" are contaminated by other conditions and are of questionable diagnostic status, so as to be untrustworthy choices for research studies.

The necessity for a replicable method is obvious in any scientific endeavor. Our laboratory carefully evaluated reported techniques, including the "minimum EEG threshold change" of Ziskind,[14] the "myoclonus and polyspike" end-point of Gastaut,[1] and the appearance of "any marked EEG abnormality or seizure" taken as end-point by Leiberman and Hoenig.[6,20] Rigid controls were included for possible errors arising from changes in blood sugar, weight, age, menses, rate of injection, ambient light, unpredictability of pentylenetetrazole (Metrazol), rate of injection, and interference by medication and therapeutic convulsions. A method was finally obtained with a "multiple-sign end-point" by Ulett et al. which survived in statistical tests for validity and reliability.[17] Inattention to some of the above sources of error may account for differences of opinion heretofore reported in the literature.

Summary

The convulsive threshold by photopharmacologic measurement of 30 carefully selected schizophrenics was not different from that of 20 nonschizophrenics.

No significant change in threshold occurred in 11 schizophrenics with improvement in clinical status.

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"Animal Hypnosis" (*Totstellreflex*) as Experimental Model for Psychiatry

Electroencephalographic and Evolutionary Aspect

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The evolutionary aspect has a wide field of application in medicine, especially where functions of the organism are concerned, and the evolutionary method has helped to gain a number of significant facts for physiology, as well as for pathology. This method may, especially if combined with other methods, contribute to a deeper understanding of the mechanism of some of the psychiatric syndromes, primarily those which have an analogue, or even a homologue, in phylogenesis or ontogenesis.

As is well known, the basic types of reactions, which are common both to man and to animals, were designated by Kretschmer [6] as "biological radicals." The "motion storm" (*Bewegungssturm*) and the so-called animal hypnosis, also called *Totstellreflex*, are such "biological radicals." Both are antipolar, phylogenetically old reactions with different forms of manifestation in animals and in man.

The "motion storm" may be encountered in hysterical hyperkinesis: in sudden affective crises, as runs in a dreamy state, in hysterical seizures, in fits of tremor, and in convulsions. Hysterical "motion storms," on the one hand, merge into acute syndromes of fear, uneasiness, and panic, and, on the other, hold a firm relation to normal child affective paroxysms. This overproduction of rapid movements repeated paroxysmally is well known, for example, from the behavior of a captured animal, which runs aimlessly about, tosses about, turns over, beats around, and screeches.

Received for publication Nov. 15, 1956.

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The second typical animal reaction to situations which endanger it, or which unfavorably change its environmental condition, is, according to Kretschmer, the so-called animal hypnosis. The symptomatology of this widespread animal instinct is very rich, from simple hiding between stones, to creeping in the sand, to hypnoid states, such as stupor and dreamy states. The last two reactions are known as the response to strong affective stimuli, especially in human hysteria (Kretschmer [5]).

The occurrence of these reactions in man and in animals makes it possible to study the mechanism of these reactions in experimental animal models, often with better prospects of success than in man (e. g., de Jong [2]). This is because the animal represents a much simpler and more comprehensible functional structure, and besides this it offers greater experimental possibilities. The evolutionary aspect of a certain human reaction would not, furthermore, be apparent without a study on animals.

My colleagues and I take the liberty of submitting a part of our experiments on animals that were intended as a study of those clinical syndromes the experimental model of which may be considered to be one of Kretschmer's already mentioned "biological radicals"—the so-called animal hypnosis. The evolutionary and electroencephalographic methods were used in the study of the mechanism of this phenomenon.

In the first part (A) of this report EEG changes during "animal hypnosis" are studied, together with the influence of arousing stimuli on the EEG record of "animal hypnosis." In the second part (B) the phy-

logenetic and ontogenetic aspects of "animal hypnosis" are analyzed.

Methods

"Animal hypnosis" was elicited by standard rotation of the animal about its vertebral axis, from the zero position of Magnus to the position of 180 degrees. The rotation was performed in a special apparatus (Svorad[11]), and each animal was rotated 10 times. The absence of mesencephalic righting reflexes was used as a criterion of the "animal hypnosis" elicited, i. e., the loss of normal quadrupedal posture, which manifests itself in the fact that the animal remains lying on its back, in a position which is incompatible with the conscious state of the animal.

The electroencephalographic investigations were performed on 29 rabbits of the same strain. The recording steel-needle electrodes were implanted into the bone in the frontal, parietal, occipital, and temporal regions, according to the craniocerebral topography of the rabbit, after preparation of the soft coverings of the skull. Bipolar leads were used, and the record was registered by means of a six-channel electroencephalograph, with ink registration. In every animal the EEG was repeatedly recorded in the waking state and during "animal hypnosis." The EEG of natural sleep was registered in five rabbits, and those of a barbiturate, 200 mg. administered intravenously, and ether narcosis (animals weighing 3.0-3.4 kg.) in an additional two groups, comprising five animals each.

Experiments on the evolutionary aspect were performed on adult representatives of individual classes of vertebrates possessing the neocortex, i. e., beginning with the reptiles. The green lizard (Lacertaviridis) represented the reptiles, and the cock the birds. Work was performed on some lower mammals (rabbit and rat), as well as on a representative of the higher mammals (cat). Experimental groups comprised 10 animals. The ontogenetic development of "animal hypnosis" was observed on groups of 10 rats between the 1st and the 18th day after birth.

Results

A. The time course of "animal hypnosis" in the EEG record is principally identical with the record of natural sleep (Fig. 1). After the rotation of the animal about its vertebral axis changes in the EEG record take place. It might be expected that the EEG would register from the very beginning the motor inhibition of the animal that occurs immediately after the rotation. This is not the case, however. While the animal is already motor-inhibited, the EEG is still registering waking activity or there is only an initial increase in the frequency. It is not until several seconds later that the EEG registers changes characteristic of falling asleep. Normal waking activity is gradually lost and is replaced by waves of lower amplitude and higher frequency. This irregular rhythm is occasionally interrupted by waves of normal frequency. In some leads short bursts of waves (spindles) are superim-

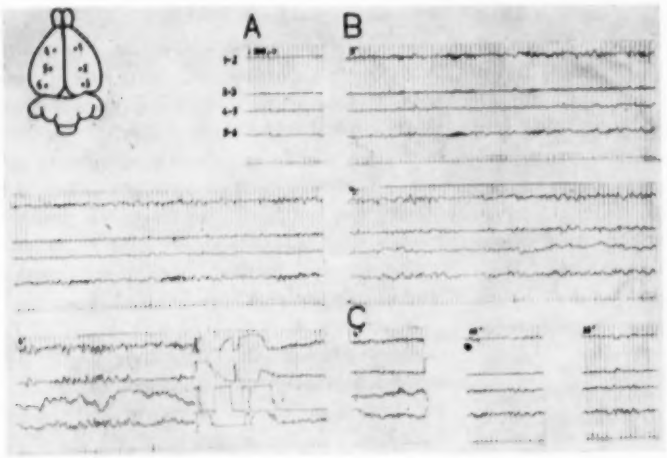


Fig. 1.—EEG record in the rabbit during "animal hypnosis." *A*, wakeful rhythm. *B*, development of inhibition after rotation of the animal about its vertebral axis (after elicitation of "animal hypnosis"). At the end, reaction of motor arousal. *C*, record after arousal from "animal hypnosis."

posed on atypical slow waves of small amplitude. Later, more and more waves of low frequency and high voltage can be seen. While there is still an irregular alpha rhythm in some of the electrodes, there is already in others a preponderance of waves of 1-2 cps frequency with an amplitude as high as 600μv. About one minute later there are slow waves (½-2 cps) to be seen in all the leads.

Spontaneous awakening of the animal from "animal hypnosis" elicited by our method is realized by turning the animal over from the supine position to the normal quadrupedal posture. This motor reaction is sometimes signalized beforehand by a depression of the sleep activity in the EEG record. In our experiments we succeeded in observing the arousal of animals in the EEG record 26 times, and in 11 of these cases, i. e., in about one-third, motor arousal was preceded by an EEG arousing reaction. The latter lasts 1 to 16 seconds.

After the motor arousal of the rabbit it is not possible to register normal waking activity until 10 seconds or more later. Continual orientation movements of the animal cause motor artifacts on the EEG record and do not prevent an uninterrupted study of the EEG mainfestations of the arousing. Several EEG records taken between motor artifacts show that after motor arousal a partly atypical EEG activity appears (Fig. 1).

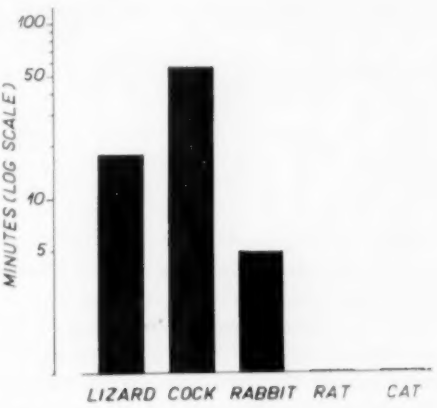
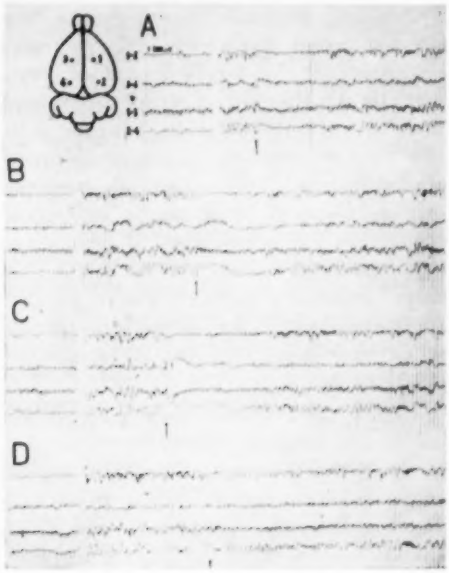


Fig. 3.—Phylogenetic development of susceptibility to "animal hypnosis," expressed as duration of this phenomenon.

Fig. 2.—EEG arousal reaction in a rabbit in "animal hypnosis." *A*, oil of cloves used as stimulus; *B*, ether stimulus; *C*, labyrinthine galvanic stimulus; *D*, visual stimulus.



The exposure of the animal in "animal hypnosis" to arousing stimuli evokes an arousal reaction in the EEG record. A considerable number of stimuli were repeatedly tested (labyrinthine galvanic, caloric, and mechanical—stimuli; nociceptive stimuli; olfactory stimuli; acoustic stimuli—noise; Galton's whistle; clapping of the hands, and visual stimuli). All the applied stimuli led to a change from the sleep electrical activity to sudden rhythm of greater frequency and small amplitude (Fig. 2). This change takes place simultaneously in all the leads, even though this depression of sleep activity is not equally conspicuous in all of them. The duration of the EEG arousal reaction differed according to the arousing stimulus used. The most effective were labyrinthine stimuli, and the least effective were visual stimuli. Motor arousal of the animal from "animal hypnosis" occurred after the application of arousing stimuli in approximately 25% of cases (EEG arousal reaction in 65.8% of 624

Values of "Animal Hypnosis" in Phylogenesis

Animal	No. of Animals	Duration of "Animal Hypnosis," Sec. (Average)	P
Lizard	10	1090±53	>0.01
Cock	10	3385±356	>0.01
Rabbit	10	317±17	>0.01
Rat	10	0	
Cat	10	0	

stimuli applied, and in 11.8% neither the EEG arousal reaction nor motor arousal was observed).

B. The development of the susceptibility to "animal hypnosis" in a phylogenetic line is shown in Figure 3. It is apparent that the longest duration of "animal hypnosis" is to be seen in representatives of reptiles and birds. Of the mammals used in our experiments, only the rabbit could be inhibited. The values of the inhibition in these experiments are shown in the Table.

The susceptibility to "animal hypnosis" decreases in the course of individual development of the rat (Fig. 4), so that, beginning with the 15th day, it is not possible to elicit this phenomenon experimentally in this animal.

Comment

A. EEG records during "animal hypnosis" have brought forward evidence that this phenomenon is real sleep and that an intense labyrinthine stimulus, i. e., sudden and rapid rotation of the animal about its vertebral axis, evokes an inhibitory process which spreads into the entire hemispheres. It is therefore more appropriate to call this phenomenon by a physiological name—paroxysmal inhibition (Svorad [12]).

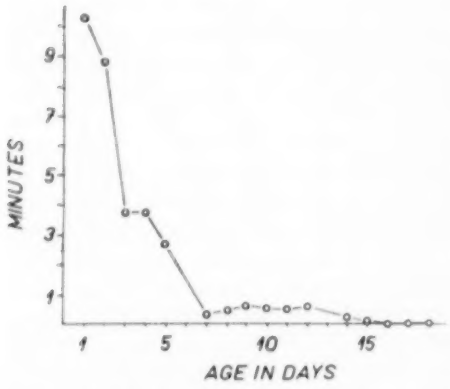


Fig. 4.—Development of "animal hypnosis" during ontogenesis of the rat.

Where does this paroxysmal inhibition originate, and from where does it spread? The comparison of reflexological and electroencephalographic data immediately after the rotation of the animal will help us to solve these questions. Although the animal loses its motor reactions immediately after paroxysmal inhibition has been evoked, i. e., at a time when it is already motor-inhibited, only electrical manifestations characteristic of falling asleep or the onset of inhibition are to be seen in the EEG. This means that if it is considered, as is usually done, that the EEG record is the electrical manifestation of neuronal activity primarily of the cerebral cortex, the loss of normal posture or of the ability to correct impaired posture occurs in consequence of the inhibition of certain subcortical regions at a time when the cerebral cortex is not yet inhibited. If the cerebral cortex was inhibited earlier, then the EEG record following rotation of the animal would not register wakeful activity, which gradually changes into the sleeping rhythm, but would, on the contrary, be manifested by waves typical of sleep immediately after the onset of paroxysmal inhibition. The EEG results, however, indicate quite the opposite. It has been demonstrated that the inhibition spreads from the original focus of inhibition, in subcortical regions, to the hemispheres of an already motor-inhibited animal, and that this inhibition of subcortical regions is also responsible for the failure of the subcortical righting reflex mechanism, i. e., for the immobility of the animal.

The results obtained while studying the influence of arousing stimuli may be helpful in elucidating the mechanism by which the animal wakens from "animal hypnosis." The simultaneous appearance of the EEG arousal reaction in all cortical regions dur-

ing "animal hypnosis" indicates that the ascending reticular activating system (Moruzzi and Magoun [9]) is functionally intact. As is well known, the ascending reticular activating system represents, in contrast with the classical sensory tract leading into primary receptor cortical areas, a secondary afferent tract with a diffuse cortical projection via thalamic and extrathalamic tracts (Starzl and Magoun [10]; Magoun [8]).

The presence of the EEG arousal reaction during "animal hypnosis" therefore shows that, even though the inhibitory focus originates in and spreads from subcortical regions, not all subcortical mechanisms are inhibited. Besides the inhibited functional units, there remain functionally intact systems important for the existence of the animal—systems which ensure the arousal from sleep. It is remarkable that this is the case not only in "animal hypnosis" but also in natural sleep. In contrast with narcosis (French, Verzeano, and Magoun [3]), the arousal from sleep is ensured in both cases.

The experiments with arousing stimuli during "animal hypnosis" indicate that peripheral sensory stimulation in the course of this inhibitory phenomenon does not rouse the animal by irradiation of the excitation from the appropriate cortical receptor area but, on the contrary, influences by a generalizated spread of the excitation from the brain stem into all parts of the hemispheres. Paroxysmal inhibition, "animal hypnosis," therefore, originates and disappears in subcortical regions of the brain.

The idea that passing to sleep and reawakening in "animal hypnosis" are of subcortical origin is plausible also in view of the facts demonstrating that certain subcortical regions, especially diencephalic reflex centers, are included in the reflex system regulating sleep and wakefulness (Hess [4]).

B. The ontogenetic development of the susceptibility to "animal hypnosis" is in general identical with the phylogenetic development; i. e., with ontogenetic, as well as phylogenetic, development this reaction is gradually lowered, until it disappears altogether.

It is possible to consider that the morphological and functional changes of the brain during evolution are the cause of these changes. It is known that with the development of the central nervous system the so-called rostral transfer of functions takes place, together with changes in the functional interrelations and in the functional significance of separate regions of the brain. For example, the mesencephalon is the leading functional unit in lower vertebrates, whereas at higher stages of phylogenesis it loses its role as coordinating center, as its former functions have been taken over by the diencephalon. The significance of the diencephalon progressively increases with higher phylogenetic forms (it is greatest in birds), but further rostral transfer of functions occurs in the mammals, so that the relationship between the diencephalon and the telencephalon of mammals is analogous to that between the mesencephalon and the diencephalon of lower vertebrates (Buddenbrock [1]). It is also known that the neocortex, which first appears in reptiles, gradually becomes functionally the most prominent part of the telencephalon. Similar changes take place during ontogenesis. In our opinion, one of the manifestations of this progressive assertion of the telencephalon and the neocortex, respectively, in the mechanisms of regulation in the organism during evolution is the different reaction of "animal hypnosis" at different stages of development.

The mechanism of "animal hypnosis," which from the evolutionary point of view is an old mechanism, the substrate of which, as has been shown by EEG analysis, is subcortical formations, is dominated by younger cortical mechanisms in the course of evolution. In consequence, the reaction of "animal hypnosis" is gradually eliminated from animal behavior in the course of the phylogenetic and ontogenetic development, until it disappears. In higher evolutionary forms it can be found only in those cases

where normal subordination relations among individual regions of the brain are impaired to such an extent that old, preformed mechanisms of lower regions come into play which under normal conditions are inhibited by evolutionary younger structures. Such a situation can develop only in pathological states, and it is for this reason that the "animal hypnosis" reaction must be considered as a pathological reaction in phylogenetically higher forms and as a phylogenetically preformed mechanism that appears in regressive forms of behavior of higher animals and of man. "Animal hypnosis"—paroxysmally initiated central inhibition—is, together with the "motor storm," a type of reaction to be met in hysteria, stupor, dreamy states, catalepsy, narcolepsy, and other symptoms of the hypnoid syndrome in human pathological behavior. It is a reaction of higher evolutionary forms wherever the relationship between the organism and the surrounding environment is not mediated by the cerebral cortex, but is mediated by subcortical mechanisms.

In evaluation of "animal hypnosis" as an experimental model for psychopathological syndromes, it is necessary always to bear in mind that we can never expect to influence the subcortical mechanisms in the way in which it is possible to do so in lower evolutionary forms. When these mechanisms are manifested under pathological conditions in higher mammals and in man, their symptomatology is poorer than should correspond (in an intact, normal organism) to their differentiated cortical functions. At the same time, they are also changed by the fact that they are no longer connected in functional unity with the other higher, intact functional units (cortex). That is why we see only remnants (Lange[7]) of earlier evolutionary forms, and that is why a general biological reaction, such as "animal hypnosis," acquires new forms in higher mammals and man when present under pathological conditions. These new forms are to be seen in the clinical symptoms of those diseases for which "animal hypnosis" may serve as a pathogenetic model.

Summary

"Animal hypnosis" (Totstellreflex), which represents one of the basic types of reactions common to man and animals, was used as an experimental pathogenetic model for the study of the mechanism of several psychiatric syndromes (catatonia, hypnoid syndrome, etc.). The course of this reaction in phylogenesis and ontogenesis was studied, and an EEG analysis was made in the rabbit.

"Animal hypnosis" is paroxysmally initiated central inhibition, which originates in the subcortical regions of the brain and from there spreads to the cerebral hemispheres. The termination of this state is realized by the ascending reticular activating system (Magoun), the function of which is not impaired in the course of "animal hypnosis."

The susceptibility of this paroxysmal inhibition to react to certain stimuli decreases in the course of ontogenesis. The same applies to the phylogenetic development of vertebrates with the neocortex. It follows that the old mechanism of "animal hypnosis," which is localized in the brain stem, is dominated during evolution more and more by younger cortical mechanisms, which progressively displace the reaction of paroxysmal inhibition from the normal animal's behavior and finally lead to its disappearance.

The opinion is expressed that the reaction of "animal hypnosis"—paroxysmal inhibition—appears in higher evolutionary forms only in the case that normal subordination interrelations of individual parts of the brain are disturbed to such an extent that old, preformed mechanisms of the brain stem, which are inhibited under normal conditions by younger functional structures, come into play or become manifest. Such a situation occurs only under pathological conditions, and that is the reason that "animal hypnosis" in higher evolutionary forms and in man must be considered to be a pathological re-

action, an instinctive, phylogenetically preformed mechanism, which appears in regressive forms of behavior.

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Diagnostic Value of Blood Pressure Responses in Psychiatric Patients

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Funkenstein and his co-workers have reported extensively upon the use of the epinephrine-methacholine (Mecholyl) test as a prognostic aid in electroconvulsive therapy,[1] but did not extend their early observation that the diagnostic grouping by this means was not a random one.[2] Hoskins commented upon sympathetic underresponsivity in schizophrenia,[3] and there are also reports of similar reduction of activity in the parasympathetic system of depressive patients.[4]

We therefore tested the blood pressure responses to these two drugs in patients with schizophrenia, endogenous depression, and mixed neuroses.

Submitted for publication Feb. 7, 1957.

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This work was carried out while one of us (D. J. L.) held a Travelling Fellowship from the R. Samuel McLaughlin Foundation, Toronto, Canada.

Present addresses: The Allan Memorial Institute of Psychiatry, McGill University, Montreal Canada (Dr. Sloane); the University of Toronto Faculty of Medicine, Department of Psychiatry, Toronto, Canada (Dr. Lewis); the Institute of Psychiatry, University of London, London, England (Dr. Slater).

Method and Subjects

This method has been previously reported.[5] All subjects were given epinephrine and methacholine (Mecholyl) on separate days.

The 21 schizophrenics ranged in age from 16 to 49 years, with a mean of 35.1 years. The 22 patients with endogenous depression ranged in age from 26 to 56 years, with a mean of 47.9 years. The 25 patients with neuroses ranged in age from 17 to 46 years, with a mean of 31.4 years. The 35 male and 33 female patients were approximately evenly distributed among the diagnostic groups.

Results

The results were scored in terms of 11 variables dependent upon the shape of the blood pressure response curve. The first three were concerned with resting blood pressure and showed no difference among the groups. The mean measurements of the other eight variables are shown in Table 1, with the F ratios and P values determined from an analysis of variance.

The differences between the depressive and the schizophrenic patients are quite large; the neurotics resemble the schizophrenics on Variables 4-9 but approach the depressives on Variables 10 and 11. The standard deviations of these measurements calculated from all 67 cases are shown in Table 2. The correlations of these measure-

TABLE 1.—*Mean Blood Pressure Measurements in Terms of Eight Variables*

Drug	Variable No.	Description of Variable	Endog. Depres.	Neuroses	Schiz.	F	P
Epinephrine	4	Maximum rise of B. P.	50.64	66.00	68.19	6.86	0.01
Epinephrine	5	Time or return of B. P. to resting level	6.77	8.29	9.33	1.55	N.S.
Methacholine	6	Maximum fall of B. P.	22.45	14.21	10.38	11.14	0.001
Methacholine	7	Time of return of B. P. to resting level (homeostasis)	12.14	8.96	5.86	3.99	0.05
Methacholine	8	Area of fall of B. P. until homeostasis	22.05	12.08	10.67	3.26	0.05
Methacholine	9	Total area of fall in 25 min.	23.68	16.62	13.00	2.05	N.S.
Methacholine	10	Area of secondary rise of B. P.	8.23	6.92	18.43	3.86	0.05
Methacholine	11	Max. secondary rise of B. P.	6.82	4.62	10.71	3.64	0.05
No.			22	24	21	--	--

TABLE 2.—*Standard Deviations of Variable Measurements in Table 1*

Variable	Standard Deviation
4	18.57
5	4.85
6	9.84
7	7.61
8	16.63
9	17.92
10	15.59
11	7.91

ments obtained from all groups are shown in Table 3.

It can be seen that these measurements fall into three classes: (*a*) Variables 4 and 5 (rise); (*b*) Variables 6, 7, 8, and 9 (fall), and (*c*). Variables 10 and 11 (secondary rise). These variables correlate generally quite highly with others in the same class but very little, and generally negatively, with the variables of other classes. This is promising for diagnostic purposes, and the measurements provide good discrimination between endogenous depression and schizophrenia, with a multiple correlation of 0.767. Optimum proportional weights for the measurements when standardized are shown in Table 4.

It can be seen that all three classes of measurements are useful, although probably a satisfactory discrimination could be worked out using only one measure from Classes (*a*) and (*c*) and two from Class (*b*).

TABLE 4.—*Optimal Proportional Weights for Variable Measurements for Table 1*

Variable	Weight
4	−0.17
5	−0.66
6	1.00
7	1.00
8	0.18
9	−0.44
10	−0.10
11	−0.72

The results for neurotics were promising, although the multiple correlations were lower, being 0.473 for discriminating them from schizophrenia and 0.553 for the comparison with endogenous depressions.

Comment

A group of patients with endogenous depression was differentiated from a group with schizophrenia by showing a lower rise of blood pressure to intravenous epinephrine and a greater and longer fall to intramuscular methacholine. The schizophrenics, in turn, were differentiated from a group of neurotic patients by showing a pronounced secondary rise of blood pressure following the initial fall to methacholine. Multiple correlations based upon measurements obtained from the blood pressure response curve were promising for diagnostic purposes, but probably of greater heuristic value. Earlier findings of a lower sympathetic response in schizophrenia and a lowered parasympathetic one in depression were not confirmed by this technique.

These findings showed that a group of patients with endogenous depression showed sympathetic underreaction and a group of schizophrenics sympathetic overreaction, as judged by this method. Gellhorn[6] interpreted such vascular responses as indicative of the degree of central sympathetic excitability and suggested that this technique might prove a sensitive indicator of such central, especially hypothalamic, responsivity. More recent work[7] has failed to demonstrate coincidental pituitary-adrenal activation following methacholine, and the postulate of a significant hypothalamic role in this test remains unproved. The sugges-

TABLE 3.—*Correlations of Variable Measurements in Table 1*

Variable	5	6	7	8	9	10	11
4	0.3859	−0.2742	−0.1980	−0.2824	−0.1884	0.0021	−0.0400
5		−0.1893	−0.2369	−0.1587	−0.1244	−0.0047	0.0383
6			0.5903	0.6681	0.6224	−0.2776	−0.3000
7				0.8793	0.8387	−0.2477	−0.3714
8					0.8989	−0.3247	−0.0003
9						−0.4123	−0.4760
10							0.8768

tion that a prolonged fall of blood pressure in depressive patients after methacholine is dependent upon excessive secretion of epinephrine, the "epinephrine-like substance" advanced by Funkenstein et al.,[8] must await biochemical confirmation.

Moreover, the known overreaction of hypertensive patients to methacholine does not seem to have contributed to this result, since the groups were not differentiated by their resting or initial blood pressures. Younger adults are probably more susceptible to the effects of methacholine than are older ones; thus, again, the greater mean age of the depressive group could not be held responsible for the overresponse.

It is even more difficult to relate the finding of an excessive compensatory rise of blood pressure in schizophrenics following the fall induced by a peripheral dilator to current theories of the relationship of schizophrenia to a hypothetical alteration in metabolism of the catecholamines arterenol and epinephrine.[9] What seems clear is that this small group of schizophrenics, the majority of whom had been ill for less than one year, did not show the sympathetic "sluggishness" reported in chronic hospitalized schizophrenics.[3] Whether this blood pressure pattern is to be regarded as no more than another example of the widened range of response found in schizophrenia or as a more specific attribute must be resolved by future work.

Summary

A group of patients with endogenous depression is differentiated from one of schizophrenics by showing a lower rise of blood pressure to intravenous epinephrine and a greater and longer fall to intramuscular methacholine (Mecholyl). The schizophrenics, in turn, are differentiated from a group of neurotic patients by showing a pronounced secondary rise of blood pressure following the initial fall to methacholine. Multiple correlations based upon measurements obtained from the blood pressure response curve are promising for diagnostic purposes.

Prof. Aubrey J. Lewis gave advice and encouragement; doctors on the hospital staffs allowed us to test their patients; nurses participated in the study, and the research committee of the Board of Governors of the Bethlem Royal and Maudsley Hospitals gave financial assistance.

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Thyroid Activity in Hospitalized Psychiatric Patients

Relation of Dietary Iodine to I^{131} Uptake

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Introduction

A number of investigators have reported abnormalities in thyroid function in mental patients. Thus, Farr,[1] Walker,[2] and Bowman and Fry[3] concluded that basal metabolic rates tended to be low in schizophrenic patients. Brody found normal levels of protein-bound iodine in 125 psychiatric patients without clinical thyroid disease. However, he felt there were small but significant differences between patients with higher and those with lower levels of tension.[4] Bowman and his associates reported increased thyroid uptake of radioactive iodine and normal protein-bound iodine in schizophrenics.[5] Cranswick confirmed Bowman's findings of elevated thyroid uptakes and lowered B. M. R.'s in schizophrenics and additionally noted in these patients an apparent unresponsiveness to hypophyseal thyroid-stimulating hormone.[6] Reiss, by tracer I^{131} methods before and after treatment, found a significant correlation between changes in mentation and thyroid function[7] which he felt was a reflection of more extensive changes in the hormone equilibrium of the patient. Zingg and Perry,[8] however, noted no difference in thyroid uptake or clearance of radioiodine between psychotic and normal euthyroid subjects.

The present investigations, conducted on patients at the Yankton State Hospital in Yankton, S. D., were undertaken with a view to extending studies on the possible relationship of thyroid dysfunction to mental disease. Preliminary findings, reported elsewhere, revealed a high proportion of elevated uptakes in the absence of any other signs of hyperthyroidism.[9,10] Inquiry revealed that the institution had never used iodized salt in cooking or as a condiment, except in the Snack Bar available to the less seriously disturbed patients. In view of the fact that the findings were consistent with iodine deficiency,[11] iodized salt was introduced throughout the hospital in November, 1955. The present report summarizes data concerning the thyroid function in patients before and nine months after the introduction of iodized salt. The results indicate that the preliminary high uptakes were due to an iodine deficiency rather than to any abnormality in thyroid function associated with the mental status of the patients.

Submitted for publication Nov. 30, 1956.

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Studies carried out during the tenure of a Lederle Medical Faculty Award (Dr. Frances O. Kelsey). Huron Clinic Foundation Fellow (Mr. Gullock).

Materials and Methods

Subjects consisted of the state hospital patients and two control series, 80 nonhospitalized subjects on whom routine diagnostic uptake studies were done, and a group of 19 healthy young men, from 21 to 27 years of age.

Each subject received 50μc of radioiodine orally and was instructed to collect all urine for 24 hours. Twenty-four hours later uptake studies were done and blood was drawn for determination of total plasma radioactive iodine, plasma protein-bound radioiodine (PBI^{131}), and plasma protein-bound iodine (PBI). The radioactivity of the urine was determined, and, in most instances, 24-hour specimens were analyzed for iodine. Tests were run Tuesday, Wednesday, or Thursday to avoid any possible effect of a fish diet on Friday. Plasma protein-bound iodine and urine iodine were determined by the method of Grossmann and Grossmann.[12] Total plasma radioactive iodine and plasma

TABLE 1.—*Uptakes Prior to Use of Iodized Salt*
(40% or More Without Hyperthyroidism)

Patient No.	Uptake, %	Time in Hospital	Age, Yr.	Diagnosis	Medication
55-126	63	3 mo.*	38	Schizophrenia, paranoid	Chlorpromazine
55-155	56	18 yr.	60	Manic-depressive, depressed	Digitoxin and aminophylline
55-122	55	40 yr.	69	Schizophrenia, simple	0
55-116	54	26 yr.	52	Convulsive disorder	Diphenylhydantoin (Dilantin)
55-166	53	8 mo.	67	Manic-depressive, manic type	0
55-159	51	1½ yr.	26	Convulsive disorder	Diphenylhydantoin
55-196	51	4 yr.	50	Schizophrenia, chronic undifferentiated	Chlorpromazine
55-191	49	7 yr.	56	Manic-depressive, manic type	Trihexyphenidyl (artane)
55-125	47	17 yr.	81	Manic-depressive reaction	Reserpine
55-157	46	3 mo.	46	Psychoneurotic disorder, anxiety reaction	Chlorpromazine
55-161	45	7 yr.	29	Schizophrenia, simple	Chlorpromazine
55-115	43	5 mo.	50	Schizophrenia, acute undifferentiated	Dicyclomine (Bentyl) & phenobarbital
55-215	43	39 yr.	60	Schizophrenia, unspecified	0
55-163	43	1 yr.	44	Schizophrenia, catatonic	Chlorpromazine
55-209	42	2½ yr.	51	Manic-depressive, manic	0
55-195	41	5 yr.	21	Schizophrenia, catatonic	Chlorpromazine
55-213	41	16 yr.	73	Mental deficiency	0
55-121	40	25 yr.	71	Involutional psychotic reaction	0

*This patient had been hospitalized elsewhere for year prior to admission to Yankton State Hospital.

protein-bound radioiodine are expressed as per cent of dose per liter of plasma.

Results

Uptake Studies.—State Hospital Patients: Uptake studies were done on 54 state hospital patients prior to the introduction of iodized salt. Nineteen of these had uptakes of 40% or higher. One of these nineteen had had a subtotal thyroidectomy for hyperthyroidism seven years previously, and her clinical picture and elevated protein-bound iodine (8.2γ per 100 cc.) were consistent with mild recurrent hyperthyroidism. In the other 18 patients, the total plasma I^{131}, the protein-bound plasma I^{131}, and the plasma protein-bound iodine were considered normal, and none manifested clinical signs of hyperthyroidism. Twenty-eight patients had uptakes of between 15% and 39% inclusive, and eight had uptakes of less than 10%. Two of these were frankly hypothyroid patients; two were on thyroid medication, while three had received iodine-containing drugs shortly before the uptake studies.

Of the 18 patients with elevated uptakes but no indication of hyperthyroidism, 10 had been hospitalized for five years or longer, and 4 for periods of one to four years. A wide variety of psychiatric diagnoses and therapeutic regimes were represented in these patients (Table 1).

Of the 28 patients with uptakes between 15% and 39%, 5 had been hospitalized for five years or longer, and 22, for six months or less, 4 of these being hospitalized for less than one month. These patients, like those with elevated uptakes, represented a wide range of psychiatric diagnoses and therapeutic regimes.

Only 13 of the patients with uptakes over 40% were available for follow-up studies after the introduction of iodized salt. The results are summarized in Table 2. The up-

TABLE 2.—*Results of I^{131} Studies on Thirteen State Hospital Patients Before and After Introduction of Iodized Salt*

Patient No.	I^{131} Uptake, %		Plasma I^{131}, %		Plasma PBI^{131}, %		Plasma PBI, γ/100 Cc.	
	Before	After	Before	After	Before	After	Before	After
55-116	54	17	0.21	0.54	0.06	0.05	5.4	7.3
55-121	40	18	0.23	0.69	0.11	0.06	5.4	6.3
55-125	47	10	0.61	1.9	0.08	0.07	6.0	7.6
55-126	63	37	0.08	0.61	0.08	0.05	5.4	6.0
55-155	56	23	0.26	0.64	0.05	0.08	6.5	10.3
55-159	51	39	0.11	0.27	0.03	0.05	6.5	5.5
55-161	45	9	0.28	1.37	0.02	0.1	6.3	7.6
55-166	53	23	0.21	0.2	0.06	0.06	6.2	8.9
55-191	49	42	0.13	0.19	0.1	0.04	6.8	9.5
55-195	42	32	0.16	0.22	0.04	0.03	6.2	8.0
55-196	51	23	0.2	0.54	0.1	0.05	6.3	7.5
55-209	42	22	0.34	0.68	0.08	0.04	5.3	7.7
55-215	43	36	0.47	0.5	0.07	0.05	5.0	7.1
Median	49	23	0.21	0.61	0.07	0.05	6.2	7.6

TABLE 3.—*Nonpsychiatric Patients with Uptakes of 40% or Higher*

Patient No.	Uptake, %	Plasma I^{131}, %		PBI, γ/100 Cc.	Comment
		Total	PBI^{131}		
54-5	77	1.05	0.39	....	Hyperthyroid, cardiovascular disease
55-234	75	0.44	0.17	4.8	Diffuse thyroid enlargement; low-salt diet
55-106	75	0.85	0.56	....	Hyperthyroidism
55-12	75	2.1	1.20	....	Recurrent hyperthyroidism
54-17	67	0.74	0.33	....	Recurrent hyperthyroidism
55-107	67	0.82	0.5	....	Hyperthyroidism
55-186	67	0.114	0.09	10.4	Hyperthyroidism
55-311	63	0.27	0.21	9	Hyperthyroid-cardiovascular disease
55-101	60	0.71	0.43	....	Recurrent hyperthyroidism
55-119	60	0.26	0.14	12	Hyperthyroidism
54-6	58	....	....	....	Had had thyroid surgery and I^{131} therapy for hyperthyroidism; clinically unimproved
55-237	55	0.53	0.38	6.1	Past I^{131} treatment; clinically improved
54-13	47	1.2	0.56	....	Nodular goiter
55-178	53	0.5	0.13	6.4	Low-iodine intake; nodular goiter
55-111	40	0.47	0.047	....	Low-iodine intake; diffuse goiter
55-263	40	0.52	0.05	8.4	Nodular goiter

takes fell within the normal range after the introduction of iodized salt in all but one patient (55-191). This patient had a nodular goiter, possibly toxic. In addition to the decreased thyroid uptake, an increase in plasma I^{131} was observed in most patients following the introduction of iodized salt. There was usually no change or a decrease in the PBI^{131} fraction.

Control Series: Of the 80 nonpsychiatric patients, 16 had uptakes of 40% or more (Table 3). In 9 of 10 patients with uptakes of 60% or higher a diagnosis of hyperthyroidism was supported by additional findings, such as clinical symptoms, plasma protein-bound I^{131} and plasma protein-bound iodine. One patient (55-234), with a diffusely enlarged thyroid, had an uptake of 75% and a somewhat elevated protein-bound I^{131} (0.17% of dose per liter). However, the protein-bound iodine was only 4.8 and the clinical findings were not typical of hyperthyroidism. This patient was on a salt-free diet for hypertension. Two of the six patients with uptakes ranging from 40% to 59% had been recently treated for hyperthyroidism with thyroid surgery and radioiodine, respectively. Three patients had nodular goiters and equivocal signs of toxicity. One of these three (55-178) was from an institution which, like the state hospital, did not employ iodized salt. One patient (55-111), with a diffuse goiter and no indication of hyperthyroidism, stated she never used iodized salt because she felt its flavor was objectionable.

Forty-five patients had uptakes of between 15% and 39%, inclusive, while 19 had uptakes of less than 15%. Of these, one was frankly hypothyroid, two had acute thyroiditis, three were receiving thyroid, one had been given a gall bladder dye a day prior to the uptake studies, and in one factitious hyperthyroidism was suspected.

The average uptake of the 19 healthy young men was 25% (range 16%-35%) and the average PBI^{131} was 0.017% of dose per liter of plasma (range 0.00-0.05%) (Table 4).

Rate of Iodine Uptake: Uptakes were done at 3, 6, 24, and 48 hours after the tracer dose in a small series of both hospital patients and normal controls. While the patients generally showed higher uptakes

TABLE 4.—*Results of Iodine Uptake Studies in Nineteen Young Male Volunteers*

	Average	Range
Thyroid uptake I^{131}, % of dose	25	16-35
Urinary excretion I^{131}, % of dose	65	41-85
Plasma I^{131}, % of dose per liter plasma	0.34	0.22-0.64
Plasma PBI^{131}, % of dose per liter plasma	0.017	0.00-0.05

TABLE 5.—*Uptakes at Three, Six, Twenty-Four, and Forty-Eight Hours in a Small Group of State Hospital Patients and Normal Subjects*

Patient No.	3 Hr.	6 Hr.	24 Hr.	48 Hr.
55-157	16	23	46	46
55-166	26	34	53	54
55-161	20	30	45	54
55-163	19	28	43	43
Control series (average of 12 subjects)	9	15	26	30
Range	7-18	12-20	20-35	23-40

TABLE 6.—*Urinary Iodide in Seven State Hospital Patients Before and After Introduction of Iodized Salt*

Patient No.	I^{131} Recovery				Urinary Iodide			
	% Uptake plus Excretion		Urine Volume		γ/100 Cc.		24-Hr. Total	
	Before	After	Before	After	Before	After	Before	After
55-116	88	59	680	400	4.0	13.8	27.2	55.2
55-124	84	87	1630	640	1.9	12.1	30.9	77.4
55-159	90	89	620	1230	3.2	5.8	19.8	71.3
55-161	86	62	800	740	3.8	12.6	30.4	93.2
55-166	88	76	1130	850	0.2	9.3	2.3	79.1
55-196	97	83	780	950	0.8	9.5	6.2	74.1
55-209	80	81	400	430	1.8	13.6	7.2	58.2

than the controls at the three- and six-hour intervals, in no instance was the peak level reached by six hours (Table 5).

Urinary Iodide.—State Hospital Patients: Urine collection could not be considered reliable in many of the hospital patients, though some indication of completeness could be gained by noting the sum of the I^{131} uptake and excretion. Despite this difficulty, an increase of urinary iodide was apparent after the introduction of iodized salt. Thus, prior to the introduction of iodized salt, the 24-hour urinary iodine in 30 patients was over 50γ in 9, between 39γ and 49γ in 8, and less than 20γ in 10. After the introduction of iodized salt, all of the 19 specimens analyzed contained over 50γ. This increase of urinary iodide following the introduction of iodized salt is illustrated in Table 6.

Control Series: Urinary iodide was determined in 46 noninstitutionalized patients. In 30 of these the total iodide was 50γ or greater; in 10 the value lay between 30γ and 49γ, and in 6 the value lay below 30γ. In two of these six subjects iodized salt was not used, and in three the analyses were invalid, owing to the presence of some substance in the urine which prevented analytic recovery of added iodide.

In 19 normal subjects, urinary iodide was determined on two 24-hour collections. The average for all determinations was 142γ, with a range of from 50γ to 193γ. The results of the urinary iodide determinations are summarized in Table 7.

Plasma Protein-Bound Iodide. — State Hospital Patients: In the 13 state hospital patients subject to uptake studies before and after the introduction of iodized salt, the median value for the plasma protein-bound iodine was 6.2γ before introduction of iodized salt and 7.6γ per 100 cc. after. In a larger series, consisting of 46 state hospital patients, the corresponding values were 5.6γ and 7.5γ per 100 cc., respectively. Practically all determinations in this larger series were run during the summer months, thus eliminating any possible seasonal influence on plasma protein-bound iodine.

Since elevated protein-bound iodine may be found in certain types of liver disease,[13] serum transaminase determinations were done on 28 of the 48 patients in order to detect evidence of acute liver disease.[14] In only one instance (Patient 55-166, Table 2) was an abnormally high value found. This patient was jaundiced, thought to be a result of chlorpromazine (Thorazine) therapy.

TABLE 7.—*Summary of Results of Urinary Iodide Determinations in State Hospital Patients and Control Subjects*

	No. of Subjects	Iodide in Urine, γ/24 Hr.			
		Above 100	50-99	30-49	Under 30
Control patients	46	14	16	10	6
Normal volunteers	19*	19	19	0	0
State hospital patients					
Before iodized salt	30	4	5	8	13
After iodized salt	19	6	13	0	0

* Two consecutive 24-hour collections.

Controls: In the 19 volunteer controls, the plasma protein-bound iodine averaged 6.2γ per 100 cc., with a range of from 5.00γ to 7.49γ. In a similar group of 25 subjects, examined a year later, the plasma protein-bound iodine averaged 6.8γ per 100 cc.

Comment

The possible role of dietary factors in the thyroid uptake of mental patients has not been overlooked by previous investigators. Thus, Cranswick[6] states that his results might be due to lowered amounts of iodine in the diets of the patients relative to the controls or to differences in concentration of antithyroid substances of vegetable origin. Bowman et al.,[5] however, state that there was no evidence of dietary lack of iodine in their patients. In the present study, although the state hospital patients represent a heterogeneous group in respect to such factors as age, sex, psychiatric diagnosis, physical condition, length of hospitalization, and medication, it is felt that no variable other than the introduction of iodized salt could explain the observed fall in radioiodine uptake and increase in plasma I^{131}, in urinary iodide, and in plasma protein-bound iodine.

As the iodine content of the drinking water at the state hospital is only 6.7γ per liter,[10] the patients must depend on food to supply the bulk of the 50γ to 150γ daily requirement of iodine. Much of the patients' food is raised locally on the hospital farm. Despite the evidence of iodine deficiency, the incidence of goiter seemed no higher in institutionalized than in noninstitutionalized patients. However, the elevated uptakes in many patients prior to the use of iodized salt and the elevated uptakes in three nonpsychiatric patients on salt-free diet or using uniodized salt emphasize the fact that this area of South Dakota lies on the goiter belt and point to the need for supplementary iodine in the diet. Furthermore, the use of uniodized salt in such areas may invalidate tracer-uptake studies in diagnosis of thyroid dysfunction.

Summary and Conclusions

Thyroid activity was evaluated by tracer radioiodine studies and by the determination of plasma protein-bound iodine in hospitalized psychotic patients; in nonhospitalized, nonpsychotic patients referred for diagnostic studies, and in a group of normal volunteers.

The high uptakes initially observed in a large proportion of the psychotic patients were shown to be due to a dietary deficiency of iodine, which was corrected by the introduction of iodized salt.

Elevated uptakes and low urinary iodide were observed in two nonpsychotic patients known not to use iodized salt, and an elevated uptake occurred in a patient on a salt-free diet.

In iodine-deficient areas, the use of uniodized salt may invalidate tracer-uptake studies for diagnosis of thyroid dysfunction.

Dr. C. Baker, Dr. O. Baum, Dr. H. Reisberg, and Dr. C. Yohe, of the Yankton State Hospital staff, cooperated in the course of this investigation.

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A Working Hypothesis as to the Nature of Hypnosis

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For half a century and more there has been a great deal written on the description of hypnotic phenomena. Since the last world war, techniques in hypnoanalysis have been described and hypnosis has become a means in helping the patient to insight. Nevertheless, there has been a conspicuous dearth of significant papers relating to the nature of hypnosis itself.

It is assumed that the real nature of hypnosis is at present unknown. This paper is offered as a working hypothesis. If it should prove untenable, it may still serve a useful purpose in diverting attention from the description of hypnotic phenomena to further inquiry as to the essential nature of the hypnotic state.

Past Theories of Hypnosis

A very significant feature of the past theories of hypnosis is that each has seemed to explain very well some particular aspect of the hypnotic state. This even applies to Mesmer's theory of animal magnetism. The patient may be hovering on the brink of hypnosis, and, at the same time, verbal suggestions are losing their effect; yet the slightest touch on the hair with the finger tips is often sufficient to send such a patient immediately into deep hypnosis. In the absence of any clear knowledge as to the mechanisms of nonverbal suggestion, it is easy to understand how our predecessors found animal magnetism a satisfying explanation of such phenomena.

Braid disproved the theory of animal magnetism and emphasized the importance of sensory fatigue in the induction of hypnosis. He believed the effect was on spinal nerve centers, which produced the hypnotic sleep. Before the introduction of dynamic methods (Meares[5]), sensory fatigue by fixation of gaze and the monotonous repetition of suggestions had been used as a mainstay for the induction of hypnosis. The explanation lies in the fact that fatigue tends to increase suggestibility in both the waking and the hypnotized subject but is not in itself an explanation of hypnosis.

Charcot's belief that hypnosis is a form of hysteria which can be induced in certain constitutionally predisposed subjects would seem to be a reasonable explanation of the hysteroid behavior of hypnotized subjects which is often such a striking feature of the hypnotic state. However, it would now appear that the hysteroid aspects of hypnosis are due to the fact that the hypnotized subject characteristically uses hysteric mechanisms to defend his ego.

These theories now belong to medical history, and the reasons for their rejection have been set out by many authors. What is the current theory of hypnosis? It would seem that most psychiatrists would still answer in the terms of Leibault and Bernheim—that hypnosis is a state of increased suggestibility. This was put forward some 60 years ago. As a psychological explanation, it was a great advance over the organic concept of Charcot, but it is only an explanation in terms of description. Increased suggestibility is the outstanding clinical feature of the hypnotic state, but no explanation of this increased suggestibility was offered.

Freud[2] postulated that hypnosis is analogous to falling in love. He thus gave some explanation for the increased suggestibility and, at the same time, explained the intensity of rapport between subject and hypnotist.

Received for publication Nov. 21, 1956.

But it would seem that Freud's theory does not account for the fact that there is very little difference in the hypnosis of male and female patients. It is also an undoubted fact that some suggestible subjects can be hypnotized against their will, and when they stand in actual fear or hate of the hypnotist. Moreover, the theory fails completely in the face of hypnosis by mechanical means, such as the metronome and Hypodisc.

Ferenczi,[1] in his psychoanalytical examination of hypnosis, regards it as a state of regression to a child-parent relationship. Although the theory explains the regression and childish behavior which often occurs in the hypnotic state, many observers must be surprised at the basic idea of the child being considered as in a state of automatic obedience to the parent. Autohypnosis presents further difficulties to this theory; and, like Freud, Ferenczi fails completely to explain hypnosis by mechanical means.

Recent investigators, apparently aware of the shortcomings of the simple and direct theories of Leibault, Freud, and Ferenczi, have abandoned simplicity and have sought the explanation of hypnosis in theories of such complexity that clarity is often obscured. Thus, two present-day authorities give explanations of hypnosis in the following terms: Guze[3] describes hypnosis as "a diffuse state of emotional readiness marked by increased tendencies for abient or adient behaviour or compensatory distortions of such activity when it cannot easily be expressed." Schneck,[7] on the other hand, states:

> The hypnotic state, in terms of its basic ingredient, is that condition represented by the most primitive form of psycho-physiological awareness of individual-environmental differentiation attainable among living organisms.

Nature of Suggestion

The word "suggestion" is used in the psychological sense as meaning the process which determines the uncritical acceptance of an idea. The essential feature of the process is that the idea is accepted in an uncritical way, and not according to its logical merits. The idea may be offered verbally, by the logical meaning of words; or it may be offered extraverbally, by the implied meaning of words; or it may be offered nonverbally, by various means, such as gesture, expression, and general behavior. If the idea which is offered is at too great variance with the logical appraisement of the proposition, then critical intellectual faculties tend to come into play and cause the idea to be rejected. When an idea is lacking in logical merit and it is accepted, it is easy to recognize suggestion as the effective mechanism; but when the idea is a sound proposition and has intrinsic logical merits which would warrant its acceptance by critical intellectual processes, then the recognition of the activity of suggestion is much more difficult. On the one hand, a sound idea may be accepted on a basis of reason according to its logical merits, or, on the other hand, it may be accepted in an uncritical way by the process of suggestion.

It becomes clear that the two processes are in some way opposed, and, furthermore, if the two processes come into conflict, the intellectual logical process is usually the deciding factor as to the acceptance or rejection of the idea. In fact, the process of suggestion is ordinarily effective only so long as the intellectual logical process is in abeyance.

Suggestion as an Archaic Mental Function

In the evolution of man, the ability of logical thought is taken to be a recently acquired mental function. In primitive man, before the evolution of logical processes, it would seem that simple ideas must have been accepted by some other, simpler, mechanism. It seems that suggestion is the process which fulfilled this function. In other words, suggestion is taken to be a primitive mental process which acted to determine the acceptance of ideas in the evolutionary period prior to man's acquisition of the ability of

logical thought. If this be so, one would expect to find evidence of the process of suggestion in the acceptance of ideas in the human infant, in primitive man, and in subhuman animal species.

The early activity of the human infant is reflex in character, but he soon begins to imitate those around him. Mother smiles, and the infant smiles back. Father holds out his hand, and the infant stretches out his tiny arm. This imitation of the infant is in response to the process of suggestion. In the examples given, the idea is offered by the expression of the mother and by the gesture of the father. This type of imitation is to be distinguished from imitation in the adult, which is often on an intellectual logical basis, in which case the process of suggestion is not involved at all. It seems that, in his imitative phase, the infant reenacts his heritage from distant ancestors of the time when suggestion ordered the life of his forebears. The primitive process of suggestion is active in infancy and childhood, only to be superseded by reason in adult life.

Like the child, the primitive is largely motivated by suggestion. In fact, it would seem that suggestion pervades the whole of primitive life. The dramatic nature of some of the findings of anthropological research has tended to divert our attention from the importance of suggestion. It must be remembered that it is only through this mechanism that animism, magic, and taboo are such a power in the life of the primitive. In the less spectacular affairs of everyday life, imitation, similar to that described in relation to the child, is active and determines much of the behavior of primitive peoples.

In the absence of clear-cut logical motivation, the cohesive force in primitive groups, which somehow produces the concerted action of individual members, must surely be suggestion. The suggestive effect of panic or rage in such groups is well known; but it would also seem that suggestion must be a major factor in the motivation of the individual's behavior in his day-to-day existence, whether it be in the method of hunting or cultivation, in the making of implements, or in the selection of food.

Observation of subhuman animal species easily discerns patterns of reaction which fall into the categories of reflex, conditioned reflex, and instinctive behavior. On the other hand, there is some behavior which is not readily explicable by these mechanisms. It often seems that an idea occurs to the animal by sight, or smell, or sound of a kindred animal; and it seems that the idea is then acted on purposefully, though uncritically, by the animal in question. The process would often seem to be one of uncritical imitation, or, in psychological terms, of suggestion. The shepherd with his dog, the teamster with his horses, are masters of communication by suggestion.

The prevalence of suggestion as a motivation for behavior in the child, in the primitive, and in subhuman species points to it being an archaic mental mechanism. The fact that suggestion is less active in modern man, and that it generally ceases to operate in the face of critical intellectual activity, points to its being superseded by the more recently acquired ability of logical thought.

Other data would tend to lend weight to this view. The theory that the more recently acquired functions are the first to suffer the effects of adverse stress has gained general acceptance. In this respect, both fatigue and sedative drugs have the effect, within certain limits, of increasing the subject's suggestibility. In other words, it seems that the noxious effect of fatigue and drugs is first manifested on the recently acquired function of logical thought, and so allows the release of the more primitive mechanism of suggestion.

Hypnosis as Regression to Archaic Mental Function of Suggestion

This concept that suggestion is an archaic mental function can be used to explain the nature of hypnosis.

The idea of regression is so generally accepted in psychiatry as to need no explanation. There is, however, one particular aspect which requires comment in the present discussion. In clinical psychiatry the term "regression" is usually applied to the return to a former type of behavior. For example, the regression of schizophrenia is seen as a return to childhood or infantile patterns of behavior. In other words, regression is usually considered in the light of behavior. It would seem that Ferenczi had this in mind when he considered hypnosis as regression to a child-parent relationship. Now, the hypothesis which is being offered requires the idea of regression to be applied, not in the field of behavior, but in the field of mental function, that is, a regression from normal adult mental function at an intellectual logical level to an archaic level of mental function in which the process of suggestion determines the acceptance of ideas. Hypnosis is considered to be the result of such regression.

This is the basic mechanism in hypnosis; but the clinical picture of the hypnotized subject is mainly determined by other mechanisms, by an overlay of other psychological processes, particularly hysteric defenses in various forms. This would seem to account for the past failures to recognize the essential element in hypnosis.

Hypothesis in Relation to Induction of Hypnosis

It would be reasonable to say that none of the past theories of hypnosis offers any satisfactory guiding principles to the clinician in his task of inducing hypnosis in his patients. The classic theory, that hypnosis is a state of increased suggestibility, leaves the problem of inducing the state of increased suggestibility to empirical techniques. On the other hand, if the hypnotic state be analogous to falling in love, then, in order to facilitate the induction of hypnosis, the clinician might be advised to form an erotic relationship with patients of either sex. But, if, with Ferenczi, the essential factor in hypnosis is a regression to childish behavior, the clinician must present himself to the patient in either a maternal or a paternal role, according to the type of hypnosis he proposes to induce.

The essence of the present hypothesis is that hypnosis is a return to a more primitive form of mental functioning in which suggestion plays a major role. This is a concept which can be of practical value to the clinician. Anything, word or act, which tends to aid this regression will aid the induction of hypnosis.

On theoretical grounds, there would appear to be three main avenues of approach. First, the newer, intellectual functions could be dulled so as to allow the older, suggestive functions free play; second, the latent suggestive functions could be stimulated and so reawakened into activity, and, third, measures could be taken to initiate general regressive mechanisms so that the specific regression of mental function might take place the more easily. It can be seen that the hotchpotch of apparently unrelated techniques which are used empirically for the purpose of inducing hypnosis fall into these three categories.

Intellectual activity is dulled by giving the suggestions in a monotonous voice, by the repetition of the suggestions, and by the sensory fatigue of Braid's method. Keeping the room warm and the exclusion of extraneous stimuli act similarly; so does the use of drugs and the various mechanical aids, such as the metronome, revolving discs, and flashing lights. In the passive induction of hypnosis, the patient is encouraged voluntarily to let himself drift into hypnosis. By the process of abandoning himself, of letting his mind go blank, he voluntarily quiets the critical faculties of the intellect, and so allows the suggestive mechanisms to come into play. Similarly, in autohypnosis, the activity of the intellect is dulled on the subject's own initiative.

The latent suggestive function of the mind is reactivated by subjecting the patient to a series of very simple suggestions. The acceptance of one suggestion seems to activate the suggestive mechanism, so that the acceptance of further suggestions is facilitated. This process is, of course, the basis of the techniques commonly used in medical practice for the induction of hypnosis.

Finally, regression to the archaic mode of mental functioning is facilitated by techniques which favor behavioral regression. In authoritative hypnosis, the prestige of the hypnotist and his assumption of authority initiate behavioral regression in the subject. The hypnotist, by presenting himself in the role of the authoritative parent, forces the subject into the role of the obedient child. This behavioral regression facilitates the regressive process, and regression in the field of mental function is so much the easier.

Hypothesis Applied to the Main Clinical Features of Hypnosis

A working hypothesis must explain the observed facts relating to the subject in question. There has been so much written about hypnosis at a descriptive level that there is now a fairly general agreement as to what constitutes the main clinical phenomena of the hypnotic state.

The increased suggestibility is the outstanding clinical feature of hypnosis. This is explained by the present hypothesis, which regards hypnosis as a state of regression to an archaic form of mental function in which behavior is mainly motivated by the process of suggestion. The suggestibility of hypnosis is the essential factor of the hypnotic state, and most of the other so-called characteristics of hypnosis are secondary features, the product of the ordinary psychodynamic mechanisms operating on this basis of increased suggestibility.

The rapport between subject and hypnotist is a constant feature of hypnosis. It is assumed that rapport is a manifestation of love in the psychological sense of the word. Some degree of rapport must be present for the primitive process of suggestion to function properly. This would seem to be a biological necessity. In general, suggestions must be accepted only from those to whom we are friendly. If this were not so, disastrous results would follow from the acceptance of ideas from those ill-disposed toward us. This is consistent with our observations of suggestion in ordinary life. In all manner of minor matters, we are continually accepting suggestions from our friends and those whom we hold dear to us, while, without the process entering our clear consciousness, we ignore suggestions from others.

Some degree of spontaneous amnesia has often been regarded as an essential part of hypnosis. In actual practice, there is a great variation in the amnesia. Some patients retain a clear memory of all of the hypnotic procedure, whereas others have a complete black-out of the whole session. In medical hypnosis, the degree of spontaneous amnesia is greater when there has been a disclosure of psychologically traumatic material. Furthermore, when the spontaneous amnesia is partial, it usually has a patchy distribution, so that the patches of amnesia cover the more traumatic disclosures. In such circumstances, the amnesia is clearly purposive and acts an an unconscious defense mechanism against the too sudden awareness of the traumatic material. Similarly, in other circumstances, the amnesia would seem to act as a defense against the unpalatable awareness that ego control had been lost. Hypnosis favors the operation of this defensive amnesia, but it is not an essential element of the hypnotic state.

Braid was so impressed with the tendency of the hypnotized subject to sleep that he regarded hypnosis as a form of sleep. Bernheim emphasizes sleep in his classic description of the induction of hypnosis. So long as hypnotists held this view, suggestions of sleep were given or implied, and the patient went to sleep in direct response to the suggestions. It is now common experience

that people can be deeply hypnotized by active methods, such as arm levitation, without going to sleep. This would indicate that sleep is not an essential feature of the hypnotic state. However, it is interesting to note that patients who are hypnotized without going to sleep, if left to themselves, will very often drift into a deep hypnotic sleep quite spontaneously. There would seem to be two explanations for spontaneous sleep in hypnotized patients. Sometimes sleep is quite purposefully used as a defense. For instance, if a hypnotized patient is being encouraged to disclose repressed psychic material by means of painting, it is not uncommon for him to fall asleep, and so defend himself from the disclosure of painful repressed material (Meares[4]). In other cases it seems that the patient believes that hypnosis is associated with sleep. Such a belief is not suggested by the hypnotist, but originates prior to the hypnotic session, and it acts in a way similar to suggestion in modifying the patient's behavior under hypnosis.

Hypnotic behavior is often characterized by its hysteroid nature and the tendency for the patient to act a part. It has been demonstrated that this behavior is capable of meaningful interpretation, and that it usually functions as a means of nonverbal communication or as an ego defense (Meares[6]). As such, it is not an essential part of the hypnotic state. However, hypnosis seems to favor the use of the hysteric defense. Many patients who in their waking state habitually use other defenses, such as obsessive-compulsive mechanisms, when hypnotized, behave as florid hysterics.

Regression, in the behavioral sense of the word, is a prominent clinical feature of the hypnotic state. It may be of two kinds, suggested or spontaneous. Suggested regression requires no further explanation. On account of the difficulty in excluding extraverbal and nonverbal suggestive mechanisms, there has been some doubt as to the reality of spontaneous regression. The importance of identification and transference, as outlined by Ferenczi, has already been emphasized. The hypnotist assumes a parental role, either paternal and authoritative or maternal and passive. The subject accepts this; and while the hypnotist stands in the position of parent, the subject is automatically placed in the position of a child. Identification and transference in this way initiate a behavioral pattern of regression. Thus, behavioral regression is looked upon as a secondary characteristic of hypnosis, determined by ordinary psychodynamic processes. In contrast to this is the mental regression to primitive function which is the essential factor of hypnosis.

The hypnotized subject also shows a tendency to ventilate suppressed and repressed traumatic psychic material. In clinical practice, this ventilation is usually initiated by direct suggestion from the therapist; but it is not uncommon for patients who have not been given any such suggestions suddenly to abreact suppressed or repressed material. This is explicable in terms of the present hypothesis. The definition of suppression implies activity of the intellect in putting the unpalatable idea out of consciousness. Intellectual function is held to be in abeyance in hypnosis, so as to allow the primitive suggestive mechanisms to function. Accordingly, it must be expected that suppressed material will tend to reenter consciousness. The same line of reasoning holds for the ventilation of repressed conflicts, provided that the censor mechanism, together with intellectual function, be regarded as a recently acquired ability.

Posthypnotic suggestion is more difficult to explain, as the suggestion which is given during hypnosis is carried out later in the waking state. The idea has been put forward that the waking from hypnosis is only apparent, and that the subject really remains in a modified hypnotic state until the posthypnotic suggestion is finally carried out. This seems scarcely feasible. There are well-authenticated cases of posthypnotic suggestion being carried out many months after apparent waking from hypnosis, during which time there has been nothing to

indicate a persistence of the hypnotic state.

In respect to posthypnotic suggestion, there is some clinical evidence to indicate that an idea implanted in the mind by the process of suggestion has psychodynamic qualities which differ from those of an idea implanted by the process of logical thought. It seems that ideas which have been implanted by suggestion have a persistence about them that is lacking in ideas which are implanted by logical thought. This applies to ideas implanted at any stage in the span of life. It seems that ideas accepted at an intellectual logical level are more easily dealt with by logical mechanisms, and are not generally disturbing to the individual. It is in childhood that the suggestive process is more active; and it is the ideas associated with the conflicts of childhood which have been accepted by suggestion that are active in the production of psychoneurotic symptoms in later life. Conversely, ideas accepted by the adult are oftener accepted on an intellectual basis, and are less frequently the cause of psychoneurotic symptoms. It seems that this is a manifestation of the persistence of ideas which have been accepted by suggestion. Then, if hypnosis be considered as a regression to an archaic state of mind in which suggestion is the main mental function, it would be expected that ideas suggested in the hypnotic state would similarly have a much higher degree of persistence than any ideas accepted on an intellectual logical basis in the waking state. This persistence of the idea seems a possible explanation of posthypnotic suggestion.

Summary

None of the present theories explains all the phenomena of hypnosis. Suggestion is the process which determines the uncritical acceptance of ideas. It is shown that suggestion is particularly active in the human infant, in primitives, and in subhuman species. From this it is argued that suggestion is an archaic mental function which in past evolutionary periods has been the main means of interpersonal communication. This archaic function has been largely superseded by the more recently acquired ability of logical thought. Hypnosis is regarded as a regression to this archaic mode of mental functioning. It is shown that the various methods for the induction of hypnosis which have been evolved empirically are effective by dulling the intellect, and so allowing free play to the latent suggestive processes, or by stimulating the dormant suggestive processes into activity, or by activating regressive mechanisms, and so facilitating a return to a primitive level of mental function. Superadded to this essential regression, there is an overlay of psychodynamic mechanisms. Hysteroid defense, identification, and transference are active. This psychodynamic overlay accounts for many of the more obvious features of the hypnotic state, and has thus disguised the essential regression to the archaic level of mental function. The hypothesis is discussed in relation to the main clinical features of hypnosis and is considered to be consistent with them.

45 Spring St.

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Correspondence

PRACTICE OF PSYCHIATRY AROUND THE WORLD

To the Editor:—We refer to the article entitled "The Practice of Psychiatry Around the World," by James L. McCartney, published in the June 1956 issue of the ARCHIVES, page 648. In its account of psychiatry in New Zealand this paper contains a number of factual inaccuracies, the major ones being as follows:

The title of our association is the "Australasian Association of Psychiatrists"; there is no "Australian Association of Psychiatrists."

Psychiatric outpatient diagnostic services have been provided by the Health Department for over 30 years. The two psychiatrists mentioned as holding general hospital appointments conduct outpatient sessions for diagnosis and treatment. In the Dunedin Hospital the psychiatric department, staffed by the hospital board and the University of Otago, provides a full outpatient service, including a child guidance clinic, staffed on orthodox American or English lines. The psychiatric social worker is fully trained.

The Mental Hygiene Division of the Health Department, which controls the mental hospitals, has employed social workers for several years. Although their training is not acceptable to the Association of Psychiatric Social Workers, several hold social science diplomas.

The statement about obtaining authority for neurosurgical procedures is misleading and apparently refers to an experimental procedure. Permission from the Director General of the Mental Hygiene Division is not required for leucotomies.

The scheme for granting study leave to M. H. D. medical officers began in 1952.

If, in the future, any of your contributors should require factual information about psychiatric matters in New Zealand, our Association would be glad to provide it.

G. BLAKE-PALMER, Chairman
New Zealand Branch
J. R. E. DOBSON, Hon. Secretary/Treasurer
Ashburn Hall, P. Bag 934
Dunedin, New Zealand

To the Editor:—I should like to call your attention to the article by Dr. James L. McCartney published in the June, 1956, issue of the ARCHIVES, page 648, entitled "The Practice of Psychiatry Around the World." In that part of his paper concerning the Philippines, pages 651-652, he misrepresents not only the Philippine psychiatric workers, few as they are and working with all the handicaps their more fortunate colleagues in the United States do not experience, but also the integrity of the armed forces of the Philippines. I believe that this was the result of a "scientific method" of investigation done in a short-cut manner.

I learned later that he dropped in on our shore as a sort of traveling tourist and stayed overnight. Possibly he talked to some local psychiatric informers who happened to be antagonistic to army psychiatrists, so that, by hearsay, an authoritative story of our army psychiatry was concluded in a summary manner.

In the first place, I, who happen to be the chief of the neuropsychiatry section, am not a neurosurgeon, as alleged in his paper, but a neuropsychiatrist. I am sure every medical man understands very well the difference. In the second place, our statistics show that from Dec. 20, 1949, up to the present time (six years) we have indicated transorbital operation on only 118 patients (repeated several times in some of them) out of several hundreds of army and authorized civilian patients treated in this section. This is mentioned just to show you that we are very careful in selecting cases for research purposes.

I hope that his paper does not give the medical world misinformation regarding other countries obtained by the same method of investigation.

JAIME C. ZAGUIRRE
V Luna General Hospital (AFP)
Quezon City, Philippines

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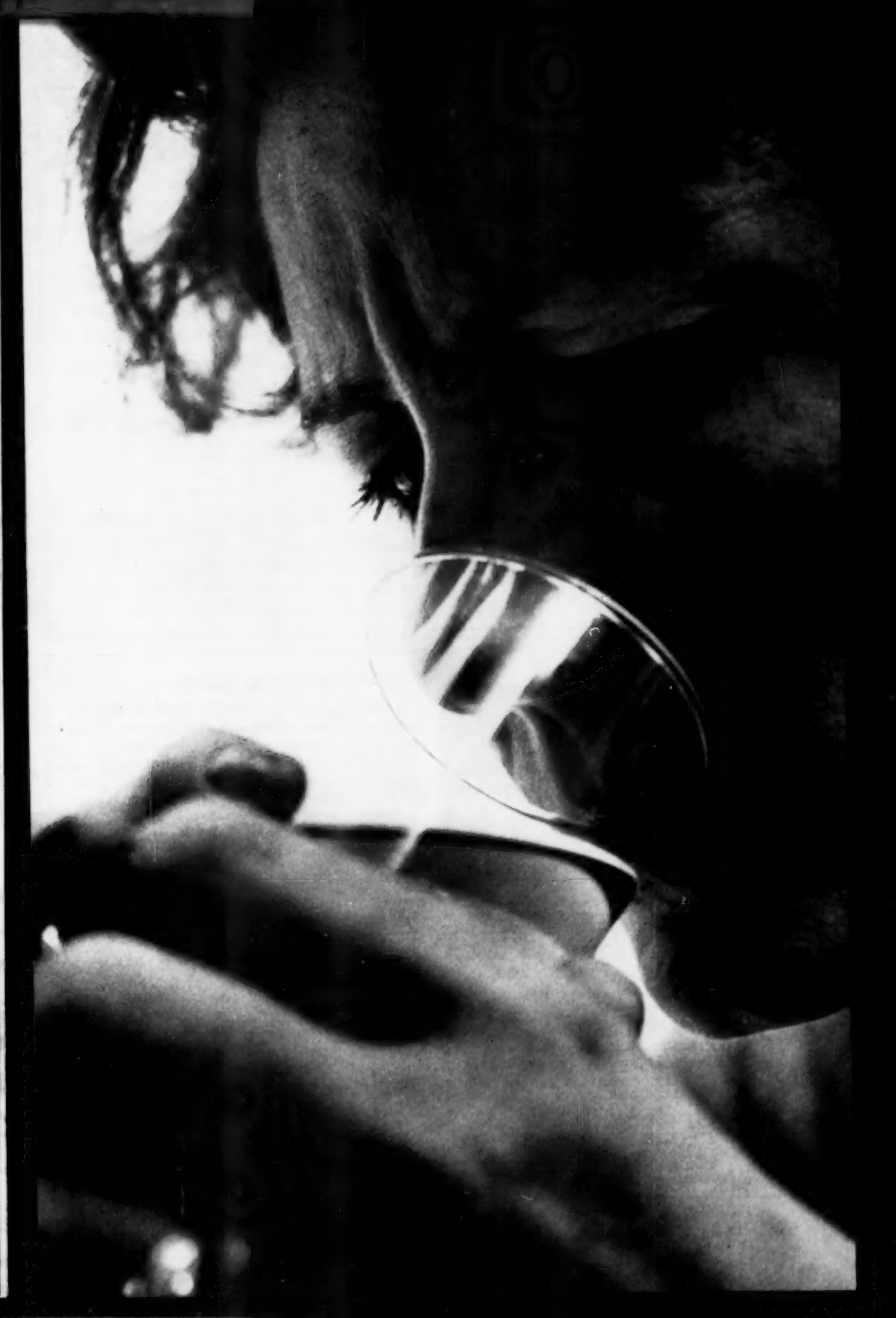

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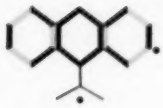

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